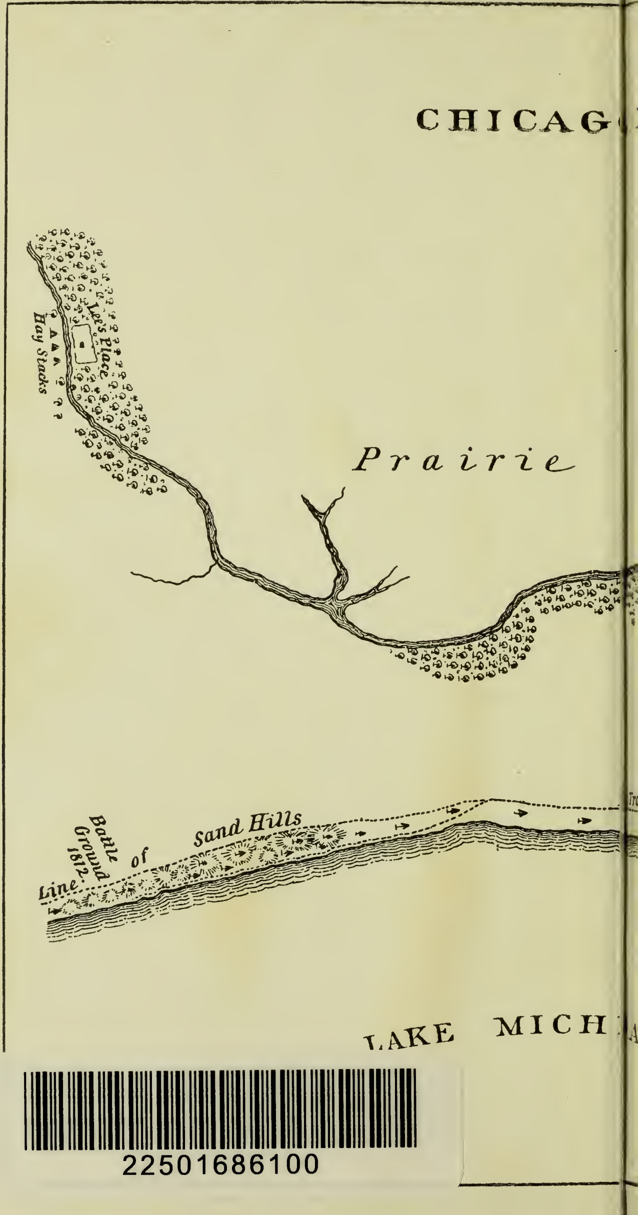
From Ergot to 'Ernutin'

An historical Sketch

Lecture Memoranda
A.M.A. Meeting
Chicago
1908

WELLCOME COLL.
/ 278



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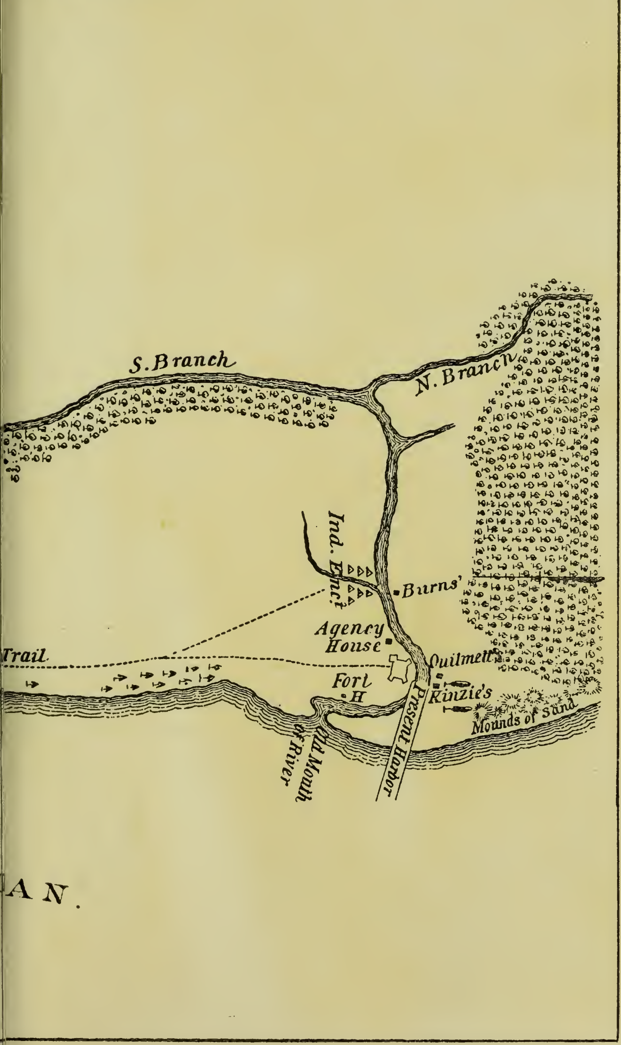
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F	3	10	17	24	31
S	4	11	18	25	..

SEAL OF CITY OF CHICAGO

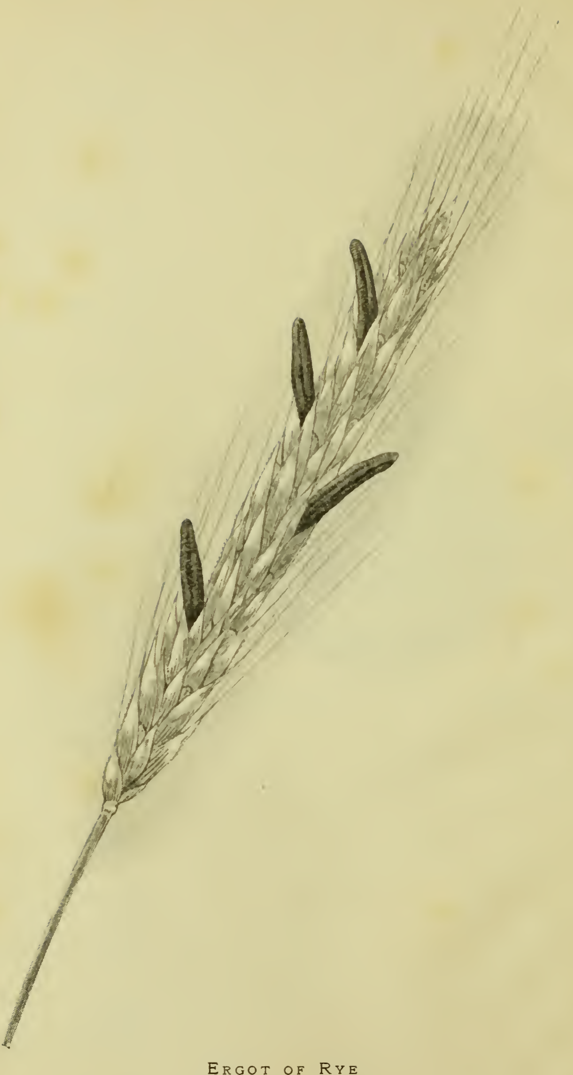
SECTIONAL INDEX

PAGE

Ergot

Botanical History 12
Chemical History 57
Early Methods of Administration 54
Therapeutic History 47

Ergot and Ergotism 18
Formulary of B. W. & Co. Products 101
From Ergot to 'Ernutin' An Historical Sketch 11
Historical Medical Equipments 65
'Soloid' Brand Products 127
'Tabloid' Brand Products 135
'Tabloid' Medical Equipments 81
'Wellcome' Brand Products 171



ERGOT OF RYE

From a recent drawing

FROM ERGOT TO 'ERNUTIN'

AN HISTORICAL SKETCH

by
C. J. S. Thompson M.B.

LECTURE MEMORANDA
American Medical Association
CHICAGO
1908

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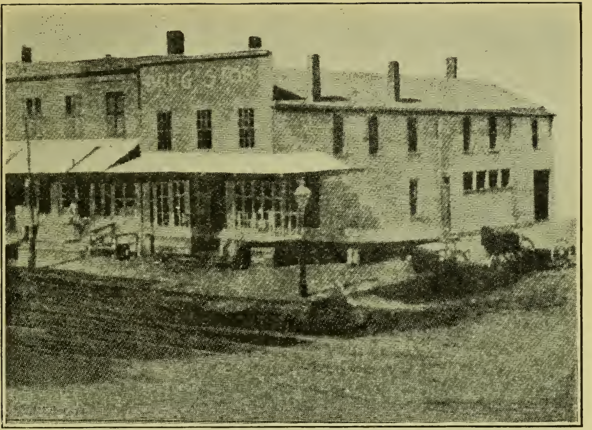
WELLCOME
COLLECTION

/ 278

INDEX

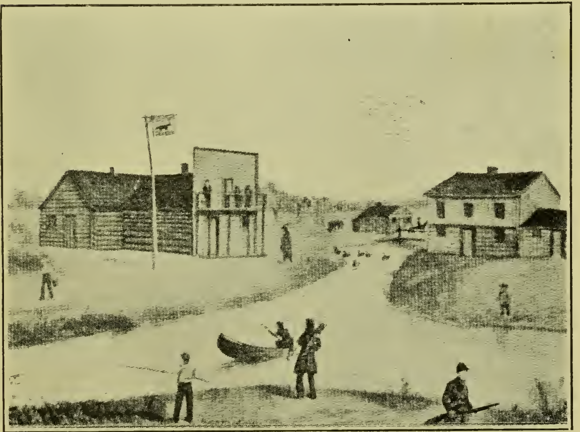
PAGE
Abu Mausur Muwaffak 13
Analysis Case, 'Soloid' Brand 95
Antidote Case, 'Tabloid' Brand 95
Bacteriological Case, 'Soloid' Brand 97
Chemicals, 'Wellcome' Brand 171
Cycle, Carriage, etc., Chests and Cases, 'Tabloid' Brand 88
"De Alimenti Facultatibus" 13
"Decoctum Parturiens" 55
Dressings, Pleated Compressed, 'Tabloid' Brand ... 103
Dressings, Surgical, 'Wellcome' Brand 105
'Elixoid' Products 106
Epidemic of ergotism in Switzerland 38
Epidemics of ergotism in Germany, etc. 33
Epidemics of ergotism in the seventeenth century ... 37
Epidemics of ergotism, Mortality from 36
Ergot, Bonjean's researches on 57
Ergot, Botanical History of 12
Ergot, Chemical History of 57
Ergot, Collection of 56
Ergot, Derivation and synonyms of 12
Ergot, Desgranges advocates the use of 50
Ergot, Earliest known allusion to 13
Ergot, Early methods of administering 54
Ergot, Fagon's description of 39
Ergot, First account of poisonous properties of 13
Ergot, Formation of 11
Ergot, Ray's allusion to uterine action of 14
Ergot, Standardisation of 60
Ergot, Stearns on 51
Ergot, Thallius notes hæmostatic properties of 14
Ergot, Therapeutic History of 47
Ergot, Tulasne's researches on 16
Ergot, Use of, in America 51
Ergot, Use of, in Europe 51
Ergot, Wigger's investigations on 57
Ergot and Ergotism 18
Ergot fungus, Villeneuve's observations on 16
Ergotinine, Tanret isolates 58
Ergotism, Antient allusions to 19
Ergotism, Earliest record of epidemic of 19
Ergotism, Effects of 34
Ergotism, Gangrenous and convulsant forms of 18

PAGE
Ergotism, "Ignis Sacer" identified with ... 43
Ergotism, Medical Faculty of Marburg investigate ... 37
Ergotism, Modern study of ... 46
Ergotism, Outbreak of, in England ... 42
Ergotism, Outbreaks of, in the Middle Ages ... 23
Ergotism, Schrine's description of ... 41
Ergotism, Sigebert's record of epidemic of ... 22
Ergotism, Tissot's account of gangrenous ... 41
Ergotism in the time of the Crusades ... 33
Ergotoxine as a medicinal agent ... 59
Ergotoxine, Barger and Carr discover ... 59
Ergotoxine: Its importance to the physician ... 60
'Ernutin' Products ... 108
First-Aid, 'Tabloid' Brand ... 98
Formulary of B. W. & Co. Products ... 101
From Ergot to 'Ernutin' ... 11
Goupil's Formula ... 54
'Hazeline' Products ... 109
Historical Medical Equipments ... 65
History of Ergot, Chronological Table of Chief Events in 61
"Holy Fire" ... 18
Hypodermic Apparatus ... 109
Hypodermic Pocket-Cases, 'Tabloid' Brand ... 81
Hypodermic Products, 'Tabloid' Brand ... 110
"Ignis Sacer" ... 18
"Ignis Sacer," Saints associated with ... 23
'Kepler' Products ... 115
Medicine Pocket-Cases, 'Tabloid' Brand ... 85
"Ocytic Potion" ... 55
Ophthalmic Pocket-Cases, 'Tabloid' Brand ... 84
Ophthalmic Products, 'Soloid' Brand ... 119
Ophthalmic Products, 'Tabloid' Brand ... 118
Pastilles, 'Tabloid' Brand ... 120
"Persian Fire" ... 19
Photographic Products, 'Tabloid' Brand ... 121
St. Antony ... 25
St. Benedict ... 31
St. Martial ... 23
Ste. Geneviève ... 31
Sanitary Towels, Pleated Compressed, 'Tabloid' Brand 125
Sera, 'Wellcome' Brand ... 126
'Soloid' Brand Products ... 127
Suppositories, 'Enule' Brand ... 106
'Tabloid' Brand Products ... 135
'Tabloid' Medical Equipments ... 81
'Valoid' Brand Products ... 168
'Valule' Brand Products ... 168
'Vaporole' Brand Products ... 169
'Wellcome' Brand Products ... 171



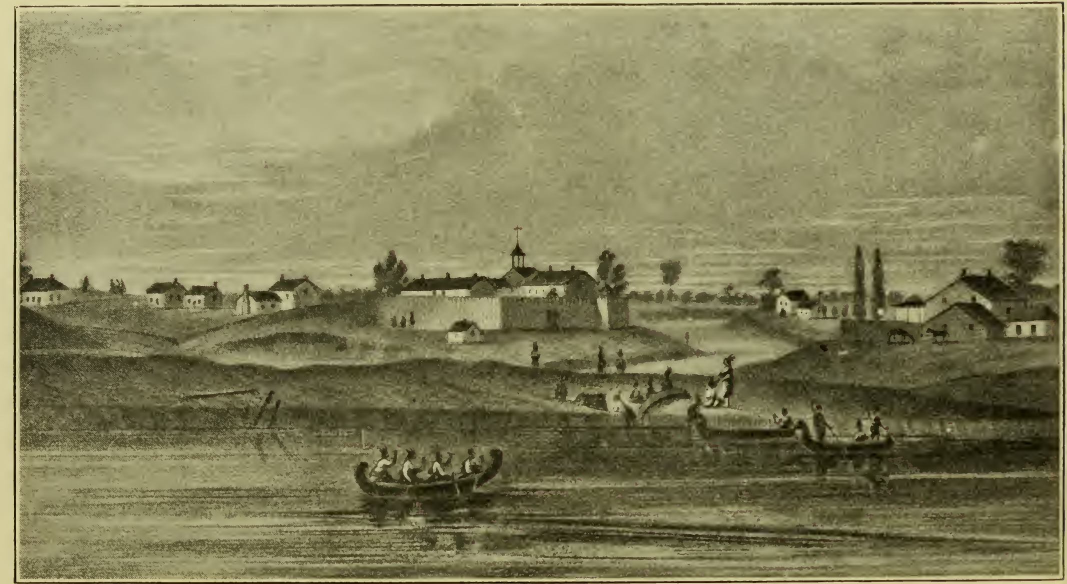
EARLY CHICAGO

The first drug store opened on the north side of the city

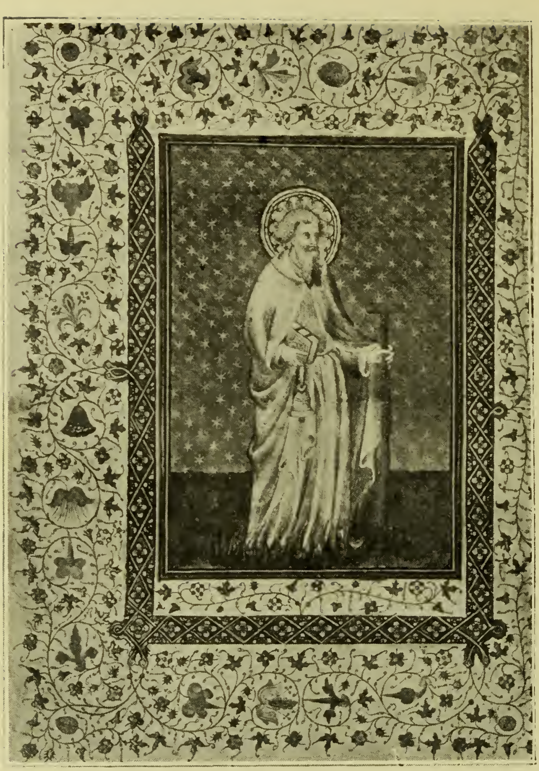


EARLY CHICAGO

"Where the brook and the river meet"



Chicago in 1820



Saint Antony

Patriarch of the monks. His relics are said to have miraculously healed many sufferers from the "holy fire," which from the eleventh century was known as St. Antony's fire. He is depicted as standing in a flaming fire, symbolical of the disease with which his name was associated, and carries his staff or crutch.

From an MS. of the XV century

FROM ERGOT TO 'ERNUTIN'

AN HISTORICAL SKETCH

Man's debt to science

THERE are few more striking examples of the debt mankind owes to medical science than that instanced in the history of ergot. From a period of remote antiquity, it is now known to have been the cause of a terrible scourge that swept away many thousands of persons, but, within the last century and a half, science has robbed it of its terrors, and has transformed it into a remedial agent of great value in alleviating human suffering.

Ergot is a peculiar form of the fungus *Claviceps purpurea*, Tulasne, being the sclerotium, or, as termed in the British Pharmacopœia, the compact mycelium or spawn which is developed in the ovaries of certain kinds of grasses. It is now obtained almost exclusively from rye (*Secale cereale*, L.), but the same or a similar fungus is produced in grasses belonging to many other genera.

How ergot is formed

The first sign of the formation of ergot on the rye is a white mould which settles on the bloom, and which is caused by the germination of the spores that have been carried by the wind on to the flowers. This mould penetrates the ovary, covering the pericarp with a soft, felt-like mass, and at the same time, a viscid substance called "honey-dew" is secreted, in each drop of which, when inspected under the microscope, a nest of conidia can be observed. These nests form into strings, and thus new masses (sphacelia) are produced. At this season, when germination takes place, there is on the ground, a small weevil, cantharis, *S. Ragonucha Melanuva fabricius*, which feeds on the honey-dew. By means of their legs and suckers they carry the conidia from one ear to another, and are thus the agents in infecting whole fields and districts. The fungus gradually develops and, by the month of June, a long, black, triangular "horn" grows out of the ear of the rye, sometimes as many as ten horns being found in one ear. This horn is the sclerotium, or final stage, in the development of the fungus.

THE BOTANICAL HISTORY OF ERGOT

Derivation of the name, and its synonyms

The word ergot is derived from the French "*argot*," "the spur of a cock," which the fungus is supposed to resemble. It has been known throughout the countries of Europe by various names, derived either from its form, origin or qualities. In France it was known as ergot, argot, bled avorte, bled cornu, bled farouche or rachitique, calcar, chambucle, clavus siliginis, clou de seigle, ebrun, faux seigle, mane, mère de seigle, secalis mater, seigle cornu or corrompu, seigle à eperon or ergotisé seigle ivre, seigle noir, secale cornutum, mater secalis and orga. In Germany it was generally called Mutterkorn, Hamelkorn, or Rockenmutter, and in England it was known as "spurred rye" or "horned rye."

Rye was one of the cereals indigenous to the Euphrates valley, and was called by the Chaldeans *Zennu*, but no mention of it occurs in the tablets at present known until about 1200 B.C.

In an inscription to Gudea on a Babylonian tablet, said to date from 2500 B.C., mention is made of "the women who gather noxious grasses, and who were expelled from the city with the exorcists and mutterers of charms."

On an Assyrian tablet, about 660 B.C., allusion is made to a "noxious pustule in the ear of grain," which may also probably refer to ergot.

In the *Yasna* part of the *Zend Avesta*, the sacred book of the Parsees, which is supposed to date from 400 B.C. to 300 B.C., there occurs the following passage: "Among the evil things created by Angro Maynes are noxious grasses that cause pregnant women to drop the womb and die in child-bed." There is little doubt this alluded to the ergotted grasses which grow commonly in the East.

The earliest known representation of Ergot of Rye (Hamelkorn)
From a woodcut, 1578

The earliest allusion to ergot is said to be in the works of Theophrastus (372–288 B.C.), who terms it *luxuries vegetum.* Pliny (A.D. 23–79) also mentions a disease which attacked corn in moist places, which may probably refer to ergot. Galen (A.D. 130), in his work *De Alimenti Facultatibus*, appears to have been aware of the danger of using diseased grain for food, and it is probable that this vitiation of grain has existed from time immemorial.

Earliest known allusion

The first clear account of ergot and its poisonous properties is given by the Perso-Arabic physician, Abu Mausur Muwaffak (A.D. 950), and, according to Mezeray, the toxic effects of spurred rye, when mixed with aliment, were also recognised by Sigebert de Gremblour in 1096, who observed that an epidemic followed the consumption of damaged crops. In Syria, ergot appears to have been employed in folk-medicine from a period of antiquity, and was known by the curious but suggestive name of "Daughter of Blood." Adam Lonicer, of Frankfort, is the next who makes mention

First account of its poisonous and medicinal properties

of ergot; in 1582 he describes its appearance in the ears of rye, and, alluding to its medicinal effects, states, "It is regarded by women to be of remarkable and certain efficacy."

It is also very clearly described in the writings of Johannes Thallius, in 1588, who states, "In Thuringia this kind of blemish is commonly called mother of rye, rockenmutter. (They use it also to stop bleeding.) I state that I observed the same kind of blemish in the year LXXV. For I found on certain mountains of Stolberg many ears of this containing not only one long, black, faulty grain of this kind, but many of them, most of them being curved in the shape of horns. At the time of florescence that year there were very heavy rains, and afterwards there came a period of very hot sunshine. Moreover, if anyone will carefully examine a single ear, the difference between the greater and lesser can easily be distinguished."

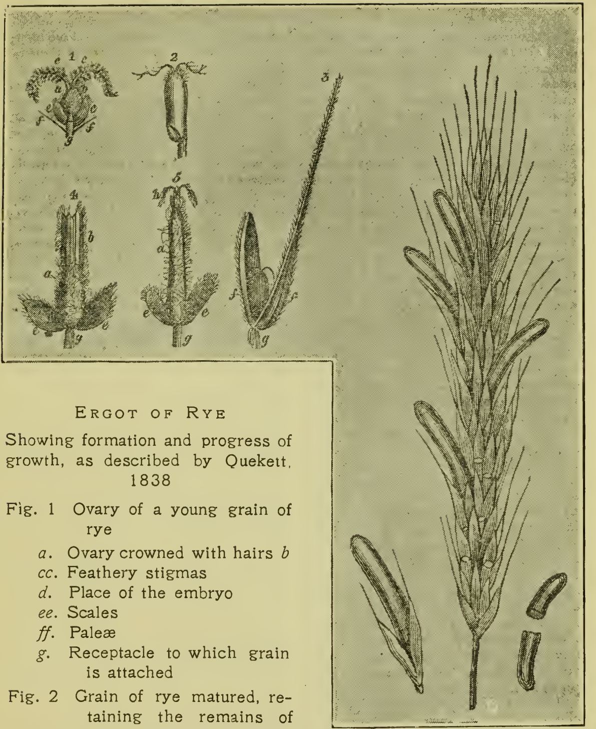
Thallius notes its hæmostatic properties

In 1623, Caspar Bauhin, alluding to ergot, cites Pliny's reference, and calls it *Secale luxurians*, while John Ray, the English botanist, in his *Historia Plantarum*, published in 1693, repeats Bauhin's description in the following words:—

"During frequent rains the lower grains of the ears of rye, when ripening, become blackish-purple. Certain seeds are pushed a long way out of their husks or glumæ, and grow rather thick. Some of them are curved into horns, which all become black on the outside, but inside contain thick, white flour. And this farinaceous substance, possessing the flavour of malt, is known by the Norici as *Mutterkorn*, *i.e.*, mother of corn, and is considered an excellent remedy for *Lochiorum fluxum*. This kind of faulty rye is called by C. Bauhin, *Secale luxurians*, and by Lonicerus, *Clavi siliginis*. Whether these excrescences owe their origin to holes made by insects of some kind remains to be discovered."

Ray's allusion to the action of ergot on the uterus

This description is especially interesting as showing



ERGOT OF RYE

Showing formation and progress of growth, as described by Quekett, 1838

Fig. 1 Ovary of a young grain of rye
- *a*. Ovary crowned with hairs *b*
- *cc*. Feathery stigmas
- *d*. Place of the embryo
- *ee*. Scales
- *ff*. Paleæ
- *g*. Receptacle to which grain is attached

Fig. 2 Grain of rye matured, retaining the remains of the stigma and hairy crown

Fig. 3 Shows position of paleæ *ff*

Fig. 4 First appearance of growth of ergot in young grain
- *a*. Ovary overrun with fungus
- *b*. Fungus has cemented anthers and stigmas together
- *ee*. Scales separated
- *g*. Receptacle

Fig. 5 Depicts the ergot now grown to show itself just without the paleæ
- *a*. Ergot beginning to turn purplish-black
- *ee*. Scales spread open
- *g*. Receptacle
- *h*. Remains of hairy crown and stigmas

Fig. 6 The ergot matured on the ear of rye

the knowledge of ergot and its medicinal properties at the close of the seventeenth century.

Villeneuve's investigations

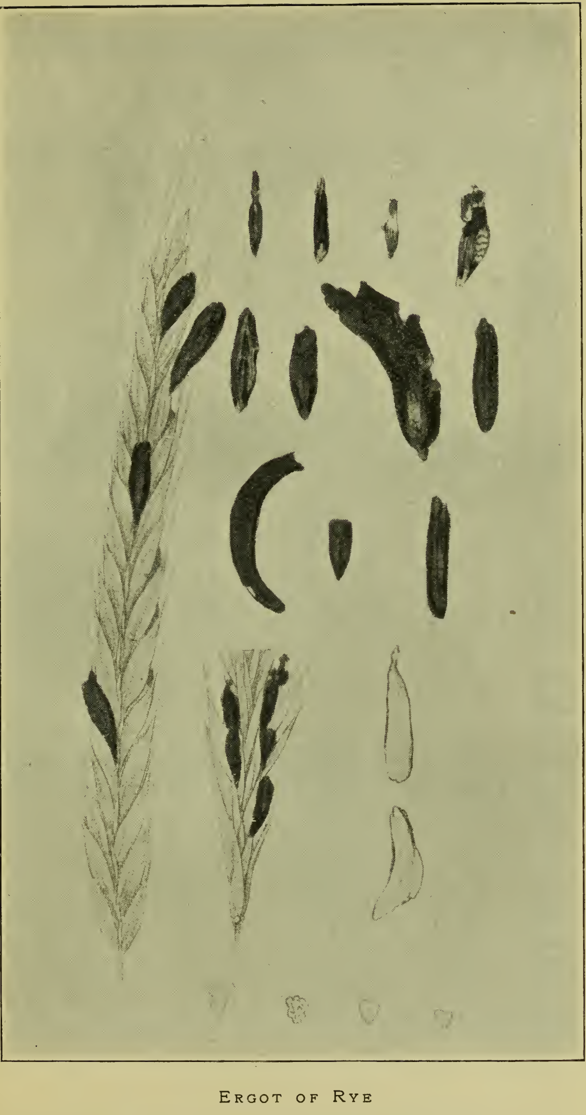
Ergot was at first regarded as a complete fungus by De Candolle, in 1816, who called it *Sclerotium clavus*. The process of the formation of ergot and its nature was first scientifically studied and investigated by Villeneuve, in 1827, who described the spurred rye as follows: "The rye grain infected by the ergot fungus is first soft and pulpy; it soon emerges from the husk, becomes firm and lengthy, and of a reddish colour, which changes to violet-black. Its growth, which is often very rapid, sometimes is such that the affected grain is very often out of all proportion to the rest of the ear."

Tulasne's researches

In 1838, Quekett read a paper before the Linnæan Society, on "Ergot of Rye," in which he traced the growth of ergot throughout its several phases. From his investigations, he concluded that ergot was a mass composed of the constituents of the diseased grain mixed with fungic matter, occupying the place of the healthy ovary. The researches of Tulasne, in 1853, were very complete and exhaustive, and these, supplemented by St. Wilson and Luerssen, practically determined our present botanical knowledge of ergot.

How Tulasne describes ergot and its formation

Tulasne showed that the fungus *Claviceps*, the mould *Sphacelia*, and spurred rye, were all different stages of the same plant. He states, "I found that the dark purplish-brown spur-shaped grains were the food-store of a fungus to which they bear a relation similar to that between the potato and the potato plant. In autumn, they fall to the ground, where they are protected from birds by their bitter taste and their colour resembling that of the soil. In spring, there arise from each 20 to 30 beautiful little pale violet fungi, the shape of round-headed pins, in the tops of which are a great number of flask-like cavities, filled with several dozen long hollow cells or



Ergot of Rye

Showing the ergot in various stages of development
From an engraving, 1838

bags, each of which contains eight slender spores; they proceed to grow out through the bags and flasks, and are then blown away by the wind. A few happen to stick in the honey-dew secreted by the flowers of grasses and grain, whereupon, particularly if they happen to fall upon the flowers of rye, they grow rapidly. Insects are thus attracted, and spores which were in them are carried to other plants.

"At the same time, the hypha penetrates the young rye grain and forms a network of dirty white fibrils outside it, throwing off fresh spores and honey-dew; the other part continues to run riot in the ovary of the rye, finally forming a compact mass of fibres; the outer layers condense into a hard purplish epidermis, and the spur is complete."

ERGOT AND ERGOTISM

The close of the seventeenth century saw the dawn of a new and important epoch in the history of ergot, when it first became seriously recognised as the cause of a pestilential disease which had ravaged the human race from the early ages. This malady, which is variously termed *ignis sacer* ("holy fire"), *ignis infernalis* ("Devil's fire"), St. Antony's fire and St. Martial's fire, is now known to have been due to the ingestion of ergotised grain, and therefore to have represented forms of the grain intoxication called ergotism.

"Ignis sacer" or "holy fire"

From various records this disease appears to have occurred in two distinct forms, namely, the gangrenous and the convulsant. The gangrenous form of ergotism, in which the circulatory symptoms are most noticeable, has been the prevalent type of the pestilence in many epidemics. The convulsant form, where the nervous system is chiefly affected, has not attracted so much attention from historians. These two forms have generally raged over distinct areas, the type of symptoms remaining constant. The difference in

Gangrenous and convulsant forms of ergotism symptoms noted in various epidemics is explained by the composition of the ergot, which, as will be shown later, may contain varying proportions of certain constituents.

Antient allusions to ergotism

Hippocrates, in his works, describes certain epidemics suggestive of ergot poisoning, particularly in his account of an epidemic which occurred in the years 347–346 B.C.; but, unfortunately, it is impossible to exactly identify the disease which the early Greeks and Romans called *ignis sacer*, or "holy fire."

According to Fuchs, the antient Greeks used the words "holy fire" to indicate several maladies, and the expression probably meant that these diseases were accompanied by burning pains, or that they perhaps spread rapidly like a fire.

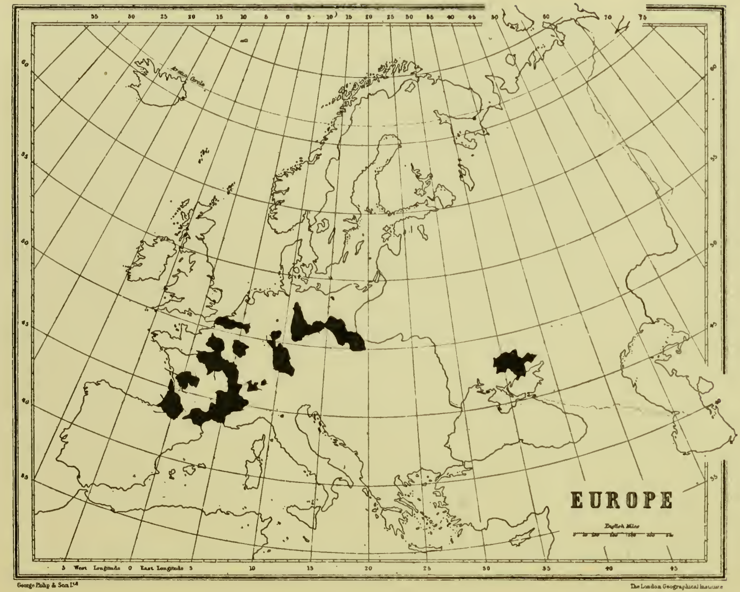
There seems to be little doubt that the malady termed *ignis sacer*, by Celsus, was really acute eczema, and that the descriptions given by Virgil and Columella under the same name referred to anthrax.

The early Arabian writers allude to a disease called "Nar-Farsi" or "Ateshi-Farsi" ("Persian Fire"); but these names are ascribed by Rhases, Avicenna and Albucasis to anthrax, measles, and sometimes to small-pox. The grievous disease which, at a later date, was known as St. Antony's fire, or St. Martial's fire, and which was probably regarded, even by physicians, as erysipelas, is now known to have been one of the forms of ergotism.

Earliest record of an epidemic of ergotism

The occurrence of ergotism in epidemic form can be traced back in France with some degree of probability as far as A.D. 857.

An interesting record of the disease is to be found in the annals of the Convent of Xanten on the Rhine, which date from the ninth century. One hundred years later the people of Paris were flocking to the churches to pray for the cure of their sufferings from the "holy fire," and in the same century, A.D. 944,



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Map of Europe

Showing the districts where, according to antient records, epidemics of ergotism occurred.

France

Artois, Paris, Lorraine, Gâtinais, Sologne, Burgundy, Lyons, Dauphiné, Perigord, Limousin, Angoumois, Landes, Aquitaine, Languedoc.

Switzerland

Zurich, Berne, Lucerne.

Belgium

Flanders, Namur.

Germany

Marburg, Hesse, Freiburg, Würthemberg, Bohemia, Silesia, Lusatia, Voigtland.

Russia

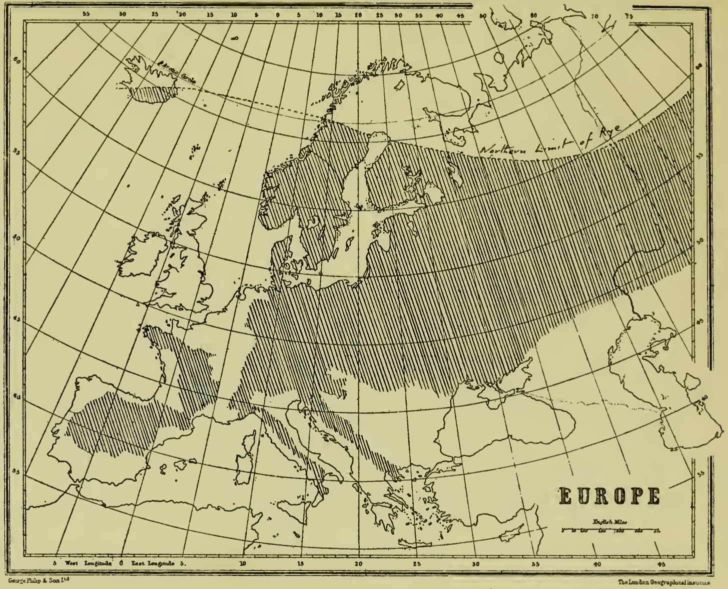
Ekaterinoslav, Kieff, Tomsk, Poltava.

Sweden

MAP OF EUROPE

Showing countries in which rye is cultivated. The shaded portions show the localities where rye is mostly grown and used as food.

ICELAND
NORWAY
SWEDEN
FINLAND
RUSSIA
POLAND
AUSTRIA
BOSNIA
TURKEY
GERMANY
SWITZERLAND
ITALY
DENMARK
FRANCE
SPAIN
PORTUGAL



it is recorded by Mezeray that a terrible outbreak of the disease called *mal des ardents*, or "holy fire," broke out in Aquitaine, Limousin, Pèrigord and Angoumois, of which 40,000 persons died. The clergy received rich donations for their intercession. It is noted, however, that the priests themselves were sometimes attacked, since the people paid their tithes in bulky ergotised grain.

Sufferings of the victims

"The cries of the sufferers were piteous," says the chronicler, "the stench of their limbs intolerable, and many were carried off in a night." Adhemar, a novice in a monastery in Angoulême, relates the same story in his chronicle. He states that the fire of the plague was noticed all over Limousin, and that a very large number of persons were afflicted by this disease, which burnt their bodies.

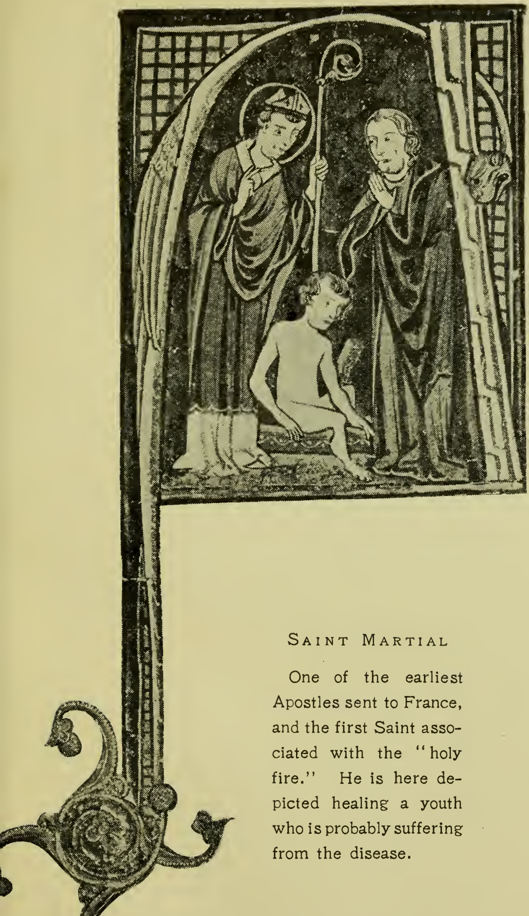
Radulf Glaber, in A.D. 994, alludes to the existence of a disease which he calls *ignis ocultus*, or "hidden fire," which, having affected a limb, separated it from the body, after having burnt it; and "the burning of their fire," he states, "consumed many in one night."

A hospital for the sufferers in Paris

Felibien, a chronicler of the tenth century, also records that during an outbreak of *ignis sacer*, according to a charter from Notre-Dame de Paris, "it was established that six lamps were to be lighted in the place where the patients were," from which it would appear that the sufferers were placed in some kind of special hospital.

It is recorded in the history of Metz, that in the year 1001, a terrible plague raged in that city, which the chronicler called "*mal des ardents;* a so terrible disease that several lost arms and legs." Again, in 1039, we learn that "a deadly burning destroyed many, both rich and poor, and left others, for example, mutilated of their limbs. There was at the same time great scarcity of corn and wine."

Sigebert gives some interesting particulars about an epidemic in A.D. 1089, which he witnessed. "In lower



Saint Martial

One of the earliest Apostles sent to France, and the first Saint associated with the "holy fire." He is here depicted healing a youth who is probably suffering from the disease.

From an MS. of the XIV century

Sigebert's record in A.D. 1089

Lorraine," he states, "a great number of people were afflicted by a gruesome disease which caused their limbs to become as black as coal, and from which the patients died miserably, or were reduced to an unhappy life, having lost hands and feet."

First named St. Antony's fire

Mezeray records an outbreak in the year 1090, and for the first time alludes to the disease by the name of St. Antony's fire. He further notes the fact that in 1096, in the Province of Namur, the bread, after being baked, appeared as red as blood. "This," he observes, "may be caused by a kind of false corn, which gives this colour to bread."

Outbreaks in the middle ages

Altogether, six great outbreaks are recorded in the tenth century, seven in the eleventh, ten in the twelfth, three in the thirteenth, the mediæval series ending with one in the year 1373.

This malady was of a nature to attract notice and to excite pity, and is frequently mentioned in the early French legends of the Saints. From the tenth to the twelfth century the term *ignis sacer* is generally used by chroniclers in referring to the epidemic, but after that period the names of "St. Antony's fire" or "St. Martial's fire" are mostly employed.

Saints associated with "ignis sacer"

Several Saints appear to have been especially connected with *ignis sacer*, and after the eleventh century their names seem to have been directly associated with the disease. This association probably originated in their acts of personal healing, or in the professed efficacy of their relics in relieving the sufferers. St. Martial appears to have been the first to perform miracles of healing from this malady.

Saint Martial

He was one of the earliest apostles of France, whither he was sent from Rome with St. Dionysius, of Paris, about the year 250. He afterwards became the first Bishop of Limoges, where, on his death, his relics were religiously preserved. It is recorded that during the first epidemic of the "holy fire" in Aquitaine the bishop carried the relics of St. Martial in procession. "When, indeed," says the chronicler, "the plague ceased at once." It may be remarked that the procession took place late in the spring, at which season the poisonous properties of ergot become attenuated.

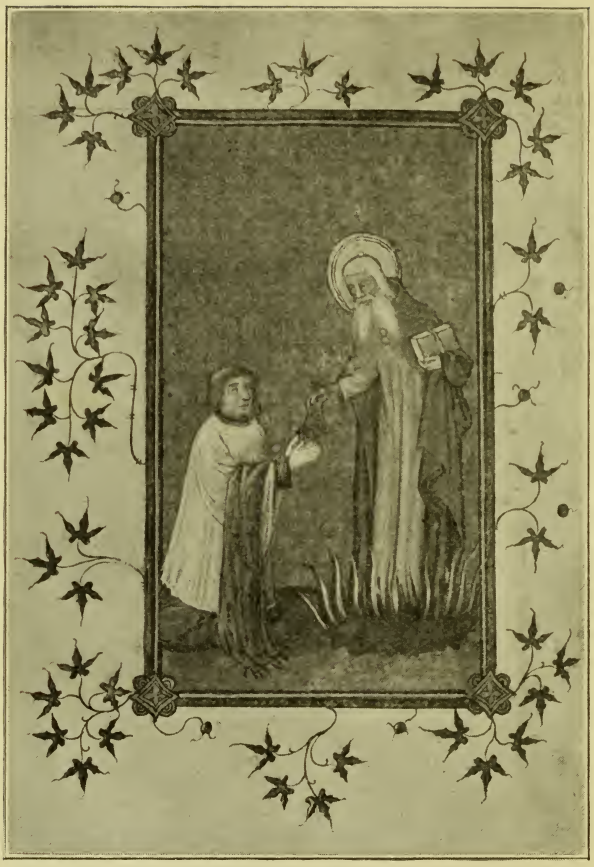
Saint Antony

The disease healed by his relics

St. Antony, who was associated with the disease which was afterwards known as St. Antony's fire, was the patriarch of the monks. His identification with the malady began, according to an ancient chronicler, in the year 1050, "when a pestilential erysipelas distemper, called 'the holy fire,' swept off great numbers in most of the provinces in France. Public prayers and processions were ordered against the scourge, and those who implored the Divine mercy through the intercession of St. Antony, especially before his relics, were speedily and miraculously healed. The church in which the relics were deposited was that of La Motte of St. Didier, situated not far from Vienne, which was resorted to by great numbers of pilgrims, and the Saint's patronage came to be implored throughout the whole country against the disease, since which time it ceased, and was known thereafter as St. Antony's fire."

How St. Antony's relics were brought to Vienne

The story how St. Antony's relics were brought to Vienne, and how the Order of the Hospitallers of St. Antony came to be founded, is related by Aymar Falco, the historian, and is not without interest. He states that, when St. Antony died, it was his wish that his burial-place should remain secret, and it was not until 170 years after his death that the place of his interment became known. He was found wrapped in a tunic, the material of which was quite different from ordinary stuff. There is no doubt that it was the garment which formerly belonged to the Hermit Paul. The remains so happily discovered were taken with great ceremony to Alexandria, and placed in the Church of St. John the Baptist.



SAINT ANTONY

The Saint is depicted standing in a flaming fire, symbolical of the disease with which his name was associated

From an MS. of the XV century

A century later the invasion of the Saracens forced the Christians to remove the relics they possessed to different countries to protect them from the profanations of their enemies. The body of St. Antony was taken to Constantinople and placed in an old church at the gates of the city.

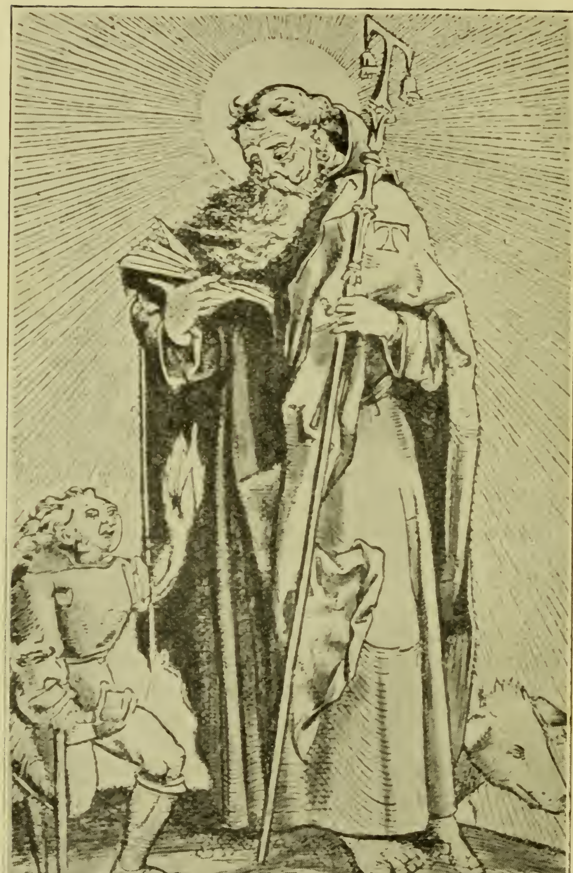
About this time a certain Jocelyn, a nobleman of Dauphiné, had vowed a pilgrimage to Jerusalem, but instead of going, occupied himself in the petty feuds common among the feudal lords of the period.

One day, being very severely wounded in a fight, he was carried for dead to a chapel of St. Antony and, reviving next morning, said he had had a vision of demons, one of whom tried to strangle him, while the rest stood ready to drag his soul to hell; but St. Antony appeared and, having driven away the devils, bade him at once fulfil his vow and, on his return, bring his relics to France, where they would receive greater honour than at Constantinople.

Saint Antony's shrine

This he succeeded in doing (A.D. 1090), and was building a church for their reception at St. Didier la Motte, near Arles, when he died childless, and his estates passed to a relative, Guy Didier, who carried the relics about with him for the protection they brought him in battle. Pope Urban II heard of this in 1095, and, much scandalised at such indecency, ordered Guy to finish the church at once on pain of excommunication, and meanwhile to put the relics in charge of the Benedictines at the neighbouring Abbey of Mont-Majour. To this he consented, and the monks established a priory there, and the shrine rapidly became famous for the cure of diseases, especially ergotism.

Amongst others came a rich man named Gaston, to pray for his son, who was sick. St. Antony is said to have appeared to him in a dream, and, after rebuking him for being more anxious about his son's body than his soul, said that God would grant his



The adoration of St. Antony by a sufferer from *Ignis Sacer* (gangrenous ergotism)

From a woodcut of the XVI century

prayer, but required them both to devote themselves and their wealth to the service of the sick. Planting his staff in the ground, St. Antony bade him and his future companions wear a blue cross shaped like its head, or the letter T, on their shoulder. Thus were the Hospitallers of St. Antony founded, and this became their badge, and probably represents the crutch used by the mutilated victims of ergotism.

Foundation of Hospitallers of St. Antony

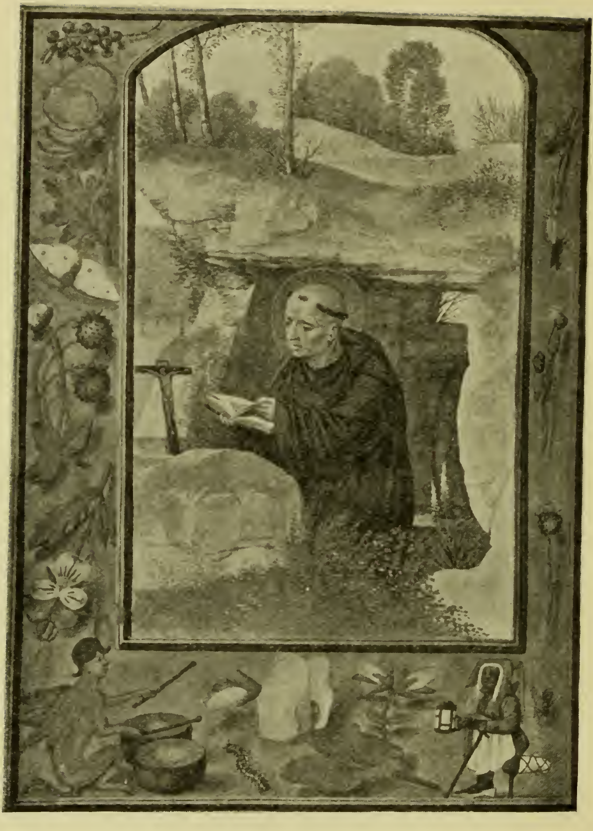
Gaston and his son, who were soon joined by others, built a hospital near the church for the reception of sick pilgrims, styling themselves Hospitallers. The community was recognised by Pope Urban in the same year, 1095, and may therefore claim to be the earliest of the Hospitaller Orders.

The second Grand Master, Stephen (A. D. 1120), built a larger hospital owing to the increased number of patients. The Order of St. Antony grew rapidly, and spread through France, Germany and Scandinavia, and acquired great wealth. The parent house was engaged in active work as late as the sixteenth century, providing food for the still numerous victims of ergotism, and affording surgical aid to the maimed who were incapable of self-support.

Faith in St. Antony's relics

In the eleventh and twelfth centuries, it was generally believed that if the sufferers from the "holy fire" could but reach the Abbey of St. Antony at Vienne, and remain there for about a week, they would be cured. Thus pilgrims made their way to Vienne from all parts of Europe, many of them, indeed, actually leaving their limbs there. Writing as late as 1702, a chronicler states, "one can still see in this abbey dried and blackened limbs kept from that time."

In all probability, the epidemics of ergotism at this period were of the gangrenous type, for in a woodcut of the sixteenth century, represented on the opposite page, is depicted the Adoration of St. Antony by a sufferer



Saint Benedict

Abbot and founder of the Abbey of Monte Casino, whose relics were believed to heal those afflicted with the "holy fire"

A watchman who has probably been crippled through ergotism is depicted in border

From an MS. of the XV century

who has lost his right foot, and who raises towards the Saint his left hand, which is represented as burning with a living flame. Beneath the original picture are the following lines:—

"O Lord Great St. Antony,
Procure us by thy sovereign grace
The pity of God, and pardon of our sin
Preserve us from thy terrible fire."

Symbols of St. Antony

It is further interesting to note that the lambent flame and the crutch are used as symbols of St. Antony, and are represented in many pictures of him executed by the monks in the middle ages. In other miniatures he is depicted as standing in a flaming fire.

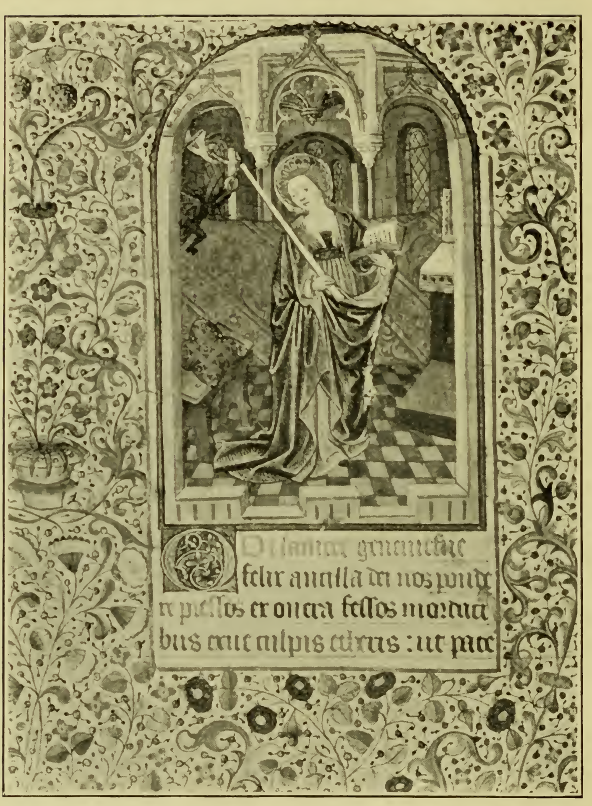
Saint Benedict

Tradition states that St. Benedict was associated with this malady. He was the Abbot and founder of the famous Abbey of Monte Casino, and was the patriarch of the Western monks. After his death his relics were visited by pilgrims suffering from the "holy fire," from which they claimed to obtain relief.

Sainte Geneviève

Ste. Geneviève, who was also connected with the disease, was the chief patroness of the city of Paris. She was born about the year 422 at Nanterre, a small village four miles from that city, and died about 512, being buried in the Church of St. Peter and St. Paul.

The city of Paris is said to have frequently received proofs of Divine protection through her intercession, the most famous instance being the miracle of "*les ardents*," or the "burning fever." In 1129, in the reign of Louis VI., it is stated that "a pestilential fever, with a violent heat and pains in the bowels, swept off in a short time 14,000 persons; nor could the art of physicians afford any relief. Stephen, Bishop of Paris, with the clergy and people, implored the Divine mercy by fasting; yet the distemper did not abate till the shrine of Ste. Geneviève was carried in a solemn procession to the cathedral. During that



SAINTE GENEVIÈVE

Chief patroness of the city of Paris. Many sufferers from the "holy fire" are said to have been healed by touching her shrine

From an MS. of the XV century

ceremony many sick persons were cured by touching the shrine, and of all that then lay ill of distemper in the whole city only three died; the rest recovered, and no others fell ill."

A chapel near the cathedral, called antiently Ste. Geneviève the Little, erected near the house in which she died, was afterwards called, from this miracle, Ste. Geneviève des Ardents.

Ergotism in the time of the Crusades

The scourge of the "holy fire" was most virulent at the time of the Crusades, towards the end of the eleventh and the early part of the twelfth centuries. Dauphiné was so smitten that Pope Urban the Second founded several hospitals of the Order of St. Antony in France.

Rabelais, who alludes to "St. Antony's fire" at the end of the introduction to Book II of his works, swears that his chronicles are the expression of truth, and threatens incredulous readers with numerous terrible diseases. He terminates his imprecations on the unbeliever with the following characteristic sentence:—

Rabelais and St. Antony's fire

"May St. Antony's fire burn you, mauditerre return to you, Lancy and malubec afflict you; may you get caquesangue and ricqueracque, fire as fine as cowhair, with quicksilver in the foundation; and as Sodom and Gomorrah, may you fall into sulphur and fire, and in the depths, if you do not firmly believe all that I want to relate in this present chronicle."

He further states that at Lyons the doors of the houses in which the sufferers lived were painted red, emblematic of the fiery nature of the disease.

Epidemics in Germany, Flanders, Burgundy and Denmark

Ambroise Parè refers to "holy fire" as erysipelas, and says that the people called gangrene "St. Anthony's fire" or "St. Martial's fire." Germany, Flanders, Burgundy, Denmark, and other countries suffered terribly from these epidemics of ergotism, but England only slightly.

The English epidemic is described as an "epidemic erysipelas, whereof many died, the parts being black and shrivelled up." Hugh of Lincoln (A. D. 1190) is said by his chronicler to have seen many who recovered from the fire at Mont St. Antoine in Dauphiné. "They were of all ages, and although terribly crippled, their health was, nevertheless, restored. Some lacked a forearm, others a leg, or even a leg and thigh up to the groin, but all their stumps were soundly healed." And so throughout the thirteenth, fourteenth and fifteenth centuries we have the same melancholy tale of the effects of this terrible scourge.

Effects of ergotism

It was even noted that the disease was most destructive in the years of bad harvests and in times of famine, but no one connected the grain with the disease.

Curious remedies for St. Antony's fire

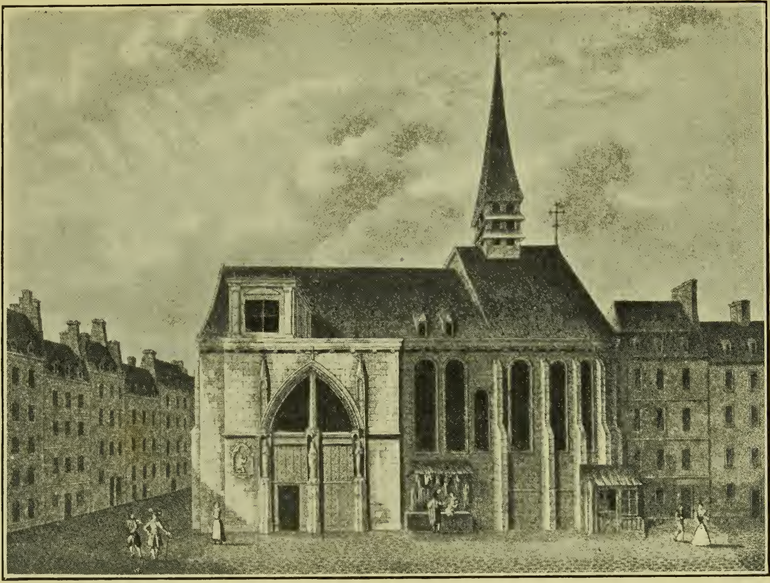
Many curious remedies were employed in the Middle Ages as cures for "St. Antony's fire" by those who had not sufficient faith in the sacred relics. A Danish manuscript of the fourteenth century gives the following recipe:—

"Against erysipelas.

"It is the 'bad fire' of bad blood. Take some hermodactyl, bones of the hen, and salt. Put together in a mortar and powder. Then wash the place of the irritation with strong vinegar and cover it with the powder. Take, too, a piece of malva, and boil the bark during two or three days. Take afterwards some earth from a molehill, and fill up the hole with all that, in order to let the flesh grow near the ulcer. After all this has been done, cover the limb to let it perspire, and the limb which falls must be placed in the sun or in the fire."

In another medical manuscript of the thirteenth century:—

"Of the plantain, his moisture is good, too, for fire in the ears and for 'bad fire.'



Church of Ste. Geneviève des Ardents, Destroyed in 1747

"Wormwood. If the leaves be cooked with oil, it is good against 'bad fire' and against what is burnt.

"Cypress mixed with barley flour and vinegar is good against 'bad fire.'"

In a medical manuscript, dated 1534, is the following recipe for "bad and wild fire":—

A recipe for the "bad and wild fire"

"If someone gets or suffers from the wild or 'bad fire,' which is called by many people St. Antony's fire, let him take some sorrel and crush it in small pieces, for the juice appeases the warmth, and cures. He must drink the juice; and also the water boiled with this sorrel appeases very well the warmth and the internal fire.

"Take the leaves and bark of the young plum-tree. Crush it in small pieces and make a plaster for the seat of the disease.

"Take the bark from the middle of the young oak, and some acorns or green acorns. Let them boil in vinegar, or water, and make with it a plaster for the same fire. This extinguishes it, and cures.

"Take some loriandre, crush it in small pieces, and make with it a plaster for the sore place, for it is very good.

"Take the root of the white lily. Roast and crush it with essence of rose, and make a plaster. On the fire and warmth let this plaster stay a long time, for it cures and is very useful. You can take also the root of the grass called 'devil-bit.' Crush it in small pieces, and place it on the same fire. It extinguishes well. You can crush the leaves of poppy with vinegar, and then place it on the part. It cures and extinguishes very well."

The same writer adds:—"If the limb of a person is inflamed with evil fire, which many persons call St. Antony's fire, let him plunge a towel into water of ribwort or plantain, for it extinguishes very well."

In the vocabulary of the manuscript *ignis sacer* is described as "a disease called 'evil fire.'"

Mortality from the epidemics

The estimates of mortality in the several epidemics of ergotism over a larger or smaller area of France range as high as forty thousand and fourteen thousand, which, however, must be taken as approximate. But in later times, upwards of five hundred deaths from ergotism have been accurately counted in a single outbreak within a limited district. The epidemics were observed to occur in particular seasons, sometimes twenty years or more elapsing before there was a recrudescence of the disease. Certain provinces were also found to be more frequently visited, notably those in the basin of the Loire, in Lorraine, and since mediæval times, especially, in the Sologne.

A contemporary description of the disease

The disease was almost exclusively confined to the peasantry, and children in particular were affected. The attack usually began with intense pains in the legs or feet, causing the victims to writhe and scream. A fire seemed to burn between the flesh and the bones, and at a later stage even in the bowels, the surface of the body being all the while cold as ice. Sometimes the skin of affected limbs became livid or black; now and then large blisters arose upon it, as in severe attacks of erysipelas. Gangrene of the extremities followed. A foot or a hand fell off, or the flesh of a whole limb was destroyed down to the bones by a process which began in the deeper tissues. The spontaneous separation of a gangrenous hand or foot was, on the whole, a good sign for the recovery of the patient.

Such was the *ignis sacer* ("holy fire"), St. Martial's fire or St. Antony's fire, which figures so prominently, and of which so many epidemics are recorded in the French mediæval chronicles.

The first suggestion that ergot was probably the cause of these epidemics was made in the year 1596, when a disease accompanied by spasms and convulsions broke out in Hesse and the neighbouring district. The Medical Faculty of Marburg, on careful investigation of all likely causes, were at length led to attribute the malady to the use of spurred rye, and in 1597 they published a tract in German on this subject, describing the symptoms, causes and methods of cure.

Ergot first identified as the cause of the disease

Sennertus, who seems to have derived his information from the Marburg report, gives the following particulars in his work on fevers: "Those who were seized with the disease scarcely ever recovered. Those who were disordered in their intellect remained so until their death. Although some lived for fifteen years after being attacked with this disorder, yet every year in the months of January and February they found themselves ill."

Thuillier, a physician to the Duke of Sully, was the first to call attention to the fact that ergot, or spurred rye, was accountable for the disease which had so devastated some parts of France in 1630. He observed that the intensity of the malady was in proportion to the amount of the vitiated grain consumed, and that the rye became spurred in damp and cold seasons. He proved the toxicity of ergot by experiments on lower animals, including birds; and his description, the result of his observation and experiment, is stated to be "the first scientific observation free from all superstition."

Thuillier's observations and experiments

Thus a great advance was made towards solving the mystery as to the cause of the epidemics.

Hoffmann states that St. Antony's fire was very prevalent in Voigtland during the years 1648, 1649 and 1675; and in 1660, 1670 and in 1674, it again ravaged some parts of Aquitaine, the Sologne and the district of Gâtinais.

Epidemics in the seventeenth century

In 1670, the Academy of Sciences in Paris, was informed of the singular effects attributed to the use of bread made from spurred rye, which had been noted in the Sologne; and six years later, Dodart was commissioned to investigate the nature of the disease caused by ergot. In addition to other observations, he concluded that ergot was most active when it was new, and lost much of its virulence as it grew stale. He also described the symptoms of the disease with considerable accuracy.

Dodart's investigations

In 1682, Dr. Bernier, a physician who had practised at Blois for twenty-eight years, published, in the *Journal des Scavans*, a short history of that city. After describing the Sologne, he refers to a "malignity which sometimes spreads itself over all the rye of this country, and which, breeding in the ears of corn certain black grains called in Sologne ergots, and in Gâtinais, *bled cornu*, does often cause dangerous diseases to the people of the country. But it is not certain that this proceeds from the soil or from the heat and moisture of the air, as was formerly said, but rather from certain hoar frosts which fall some years, and always towards the month of May."

Bernier's observations

About the same period, the Abbé Tessier noticed that the conditions preceding an outbreak of the disease were generally the same. (1) The district was damp and foggy; (2) the vegetable products were badly nourished and small; (3) the people were in bad health and reduced to want.

Tessier's investigations

In 1709, an epidemic of ergotism swept over the cantons of Berne, Lucerne and Zurich, and an accurate account of the disease was recorded by Lange, who made careful experiments with the diseased grain. He found that it abounded mostly in rainy years, and when a hot summer followed a wet spring. He speaks of the excruciating pain which preceded and accompanied the gangrene, and traces the disease to ergot, which he calls "*clavis seccalinus*."

Epidemic in Switzerland

A description of the disease in the seventeenth century

The epidemic in Switzerland spread to Dauphiné and Languedoc, and an account of it is recorded in the archives of the Abbey of St. Antoine at Vienne. It describes how the unfortunate victims were tortured for six months or more before death released them from their sufferings, and the physicians of the Abbey noted the devouring pain which burned the affected parts with intolerable agony, cold as they appeared to the touch. One chronicler describes the gangrene as of the black and dry variety, but another physician of the Abbey refers to many cases in which the gangrene was not altogether dry, but suppurated, and was accompanied by a terrible smell. Four hundred parishes were thus attacked in this part of France.

Noel's observations

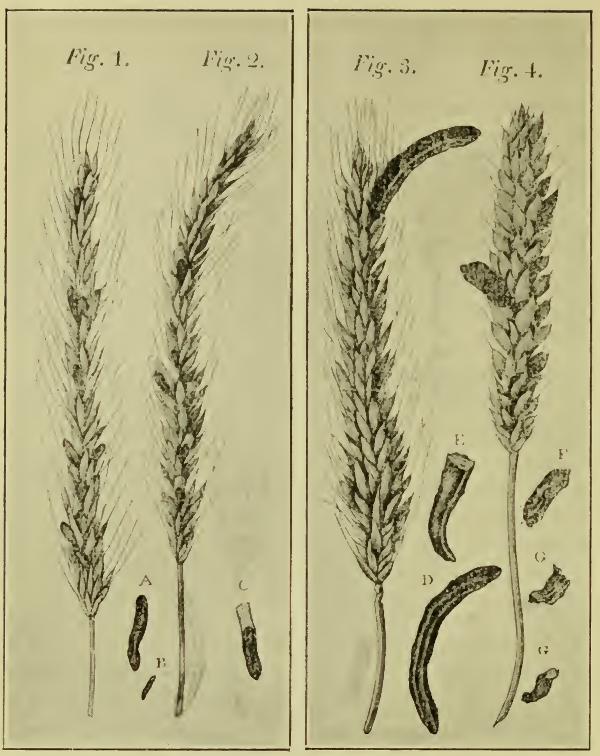
In 1710, M. Noel, a surgeon of the Hôtel Dieu at Orleans, published an article in *L'Histoire de l'Académie Royale de Science*, in which he states that "within a year's time he had received into the hospital more than fifty patients afflicted *d'une gangrène sèche, noire et livide*." He adds that this disease affected men only, and that in general the women, except some very young girls, were quite free from it. The members of the Academy were of the opinion that the disease was produced by bad nourishment, particularly by the use of bread in which there was a great quantity of ergot.

Fagon's description of ergot

M. Fagon, the chief physician to the King of France at this time, describes ergot as "a king of monsters in vegetation, which a particular sort of rye, sown in March, is more apt to produce than what is sown in the autumn, and which often abounds in moist, cold countries, and in wet seasons."

In 1710, after an outbreak of the disease in Russia, Peter the Great instructed Schober, a physician of that period, to make a study of it.

During the eighteenth century, Germany had several visitations of the disease. In the year 1702, an



Ergot of Rye

From a woodcut, 1682

Fig. 1. Ear of rye containing ergot
A—Middle sized ergot detached
B—Small ergot detached

Fig. 2. Ear containing grains composed of rye and ergot
C—Grain composed of rye and ergot

Fig. 3. Ear of stout rye containing only one large ergot
D—A great ergot detached
E—A great ergot broken transversely

Fig. 4. An ear of wheat which bears one ergot
F—An ergot of wheat out of the ear
G G—Ergot irregularly shaped

epidemic of ergotism broke out in Freiburg, and, in 1716, it is recorded by Vedelius as being prevalent in Saxony and Lusatia. In 1717, Vater states: "It appeared again in Germany, and five years later there was an outbreak in Silesia."

Ergotism in Germany in the eighteenth century

Shortly afterwards, an epidemic of the malady broke out in Saboth, which is described by Burghart; and another in Würthemberg, which is recorded by Schrine, who visited as many as five hundred patients. He vividly describes the symptoms and progress of the disease in the following words:—

"Beginning with a disagreeable titillation of the feet, as if ants had been creeping up them. This was soon followed by a violent pain in the stomach, by which both the hands and the head were affected. The titillating sensation was followed by a violent contraction not only of the hands and feet, but also of the toes. The patients exclaimed that their hands and feet were on fire, while their bodies were bedewed with copious sweats. After much pain, the head became heavy, and vertigo came on, with dimness of sight. Some either became totally blind or saw objects double. They staggered and lost their memory. Some became insane, others melancholic and comatose. In those above the age of fifteen epilepsy was liable to come on, and generally proved fatal."

Schrine's vivid description of ergotism

In addition to these sufferings, the patients were afflicted with a voracious appetite, almost impossible to satisfy. The pulse in every instance was normal and healthy. The disease lasted from two to eight, or even twelve, weeks with intermissions.

One of the most remarkable things connected with this malady was the varied and decided forms it took. Tissot gives an account of the spontaneous gangrene form, the first symptom of which was a numbness of the legs, followed by a pain, with slight swelling, but

Tissot's account of gangrenous ergotism

no inflammation. Then, in rapid succession, came coldness, lividness, mortification, and the dropping off of the legs. Among the patients afflicted in the Sologne, there was no fever, and the pains were slight. No remedies were applied, and the nose, fingers, hands arms, feet and legs, when they became gangrenous simply dropped off.

The outbreaks in Germany, Sweden and Russia were to some extent of a different type from the epidemics of gangrene common in France. The sensory symptoms were followed by a disorder of the motor system and spasms of the limbs, very often passing into contractions of the joints, which no force could unbend, and sometimes accompanied by convulsive fits of the whole body, in which the disease was often mistaken for epilepsy. This was the type called convulsive ergotism, or, in Germany, *Kriebelkrankheit.*

Severe outbreak in 1746-7

From 1746 to 1747 there were severe outbreaks of ergotism in Sweden, Russia, the Sologne, the Landes, Artois, Flanders and other places. In this epidemic, the pain seems to have been terribly violent, so that the victims in their agony hurled themselves against the walls, or even threw themselves into the water.

Slight outbreak in England

About the middle of the eighteenth century, there was a slight outbreak of ergotism in England. On the 10th of January, 1762, a family living in Wattisham, in Suffolk, consisting of the father, mother and six children, were attacked almost simultaneously with the symptoms of gangrenous ergotism, several of them eventually losing a portion of their limbs. The disease began with intense pains in the legs, and contractions of the hands and feet. It was proved that they had not been using rye flour, but that their bread for a short time before had been exclusively made from damaged wheat, grown in the neighbourhood, and kept apart from the farmer's good corn, so as not to spoil his samples. It had been sent to the mill just before Christmas, and had been used by some others besides the family, who developed the symptoms of ergotism.

England's immunity

There is little doubt that the chief reason of our immunity, in England, from epidemic ergotism has been owing to the fact that the grain was better grown in this country, and that rye was a comparatively rare crop, and seldom used for food, wheaten bread being generally preferred.

Ergot recognised as the cause of the epidemics

It was not until the end of the eighteenth century that the scientific world really awoke to the fact that there was a direct connection between the various forms of the disease which had attacked the peasantry in many countries and the vitiated rye crops; although the country people themselves and several observant medical men living in the affected districts had been alive to the fact for a considerable period.

According to Haser, it was not until the year 1771 that the identity of the old *ignis sacer* with the modern gangrenous ergotism was made clear.

"Ignis sacer" identified with ergotism

About 1783, Saillant, at the instance of the Royal Society of Medicine of France, undertook an investigation to determine whether ergot of rye was capable of producing dry gangrene or not, a question on which many observers of the period, such as Langius, Perrault, Dodart and others differed. He studied very closely on the spot the symptoms of the two distinctive forms of ergotism, and has left a valuable clinical description of the disease, and the methods of treatment used at the time.

"The dry gangrene," he states, "is characterised by the mortification of some one of the extremities, sometimes all of them. Often it is preceded by a redness, which, however, is not inflammatory, and by some vesifications. The limb swells, becomes painful, and has a sensation sometimes of cold, but more frequently of insupportable heat. The vessels are obliterated, the phlegm becomes black and hard, and the patient at the point of death is happy if, from a spontaneous separation of the gangrenous part, he can survive with the loss of his extremities.

"The first symptoms of this disease are not alarming. The pulse continues for some time nearly in the natural state, and is gradually weakened in proportion to the violence of the disease. The blood appears black and thick, and the urine in a rational condition. The belly is hard and tense, but the appetite continues, and digestion goes on as in health. It is only towards the end, and even on the approach of death, that diarrhœa usually comes on. After death, on examination of the body, the intestines and other viscera are often found strewed over with gangrenous spots.

"The cure of this disease is sometimes accomplished in the beginning by profuse sweats and by a good diet. The medical treatment consists in evacuating the *primæ viæ*, in giving internally laxative apozems, diuretics and antiseptics, while recourse is had externally to those topical applications which are proper for resisting gangrene, for favouring the separation of the diseased part without amputation, and for aiding suppuration."

After this description of dry gangrene, he proceeds to give an account of the convulsive epidemic affection :—

"In that disease," he observes, "there is not any gangrene—the violent convulsions are its essential characteristic. It has no regular course, but returns by paroxysms, and while it is in reality less dangerous than the dry variety, it yet makes its attack with much more alarming appearances. The patient at one time feels as if he were burnt with devouring fire, and soon after is sensible to cold similar to what arises from the application of water. These symptoms are accompanied by loss of appetite, nausea and vomiting, which are soon succeeded by inexpressible pain. The patient, without shedding tears, utters lamentable cries; and the affected members are either contracted with extreme violence or remain stretched out with inflexible rigidity. The pains soon abate, when the patient is able to stretch the contracted membranes or to bend those that have been stretched, but they return in a fresh accession with the same severity. The patient is no sooner out of the fit than he is tormented with a voracious appetite, and he digests with sufficient ease all sorts of aliment. In particular years there succeeds swelling of the feet and hands, and the fingers have been covered with vesicles full of serosity, the discharge of which, however, does not procure any relief. The disease, after several accessions, terminates itself by sweat or diarrhœa, which is more violent when patients eat little than when they eat a great deal. But for the most part there remains for the space of some weeks several inconveniences, such as vertigo, *tinnitus aurium*, deafness, loss or diminution of sight or the like. If the affection continues long and degenerates into epilepsy, and if during the affection there shall occur a mental disorder, it in general continues for life. If there occurs an obstruction of the liver there in general supervenes a spitting of blood, sometimes followed by phthisis, by epilepsy, palsy, or, in fine, apoplexy.

" This disease attacks most frequently those who are plethoric, and in that case the convulsions are the most violent. But those of the phlegmatic temperament are most subject to comatose affections after it.

" Some have observed blood issue from the nose and mouth, but they have not observed any alteration in the viscera, excepting that the lungs were much inflated and distended with blood. In other cases the liver and gall bladder have been much distended with the bile, and an erysipelatous inflammation has been observed over the whole surface of the abdominal and even the thoracic viscera.

" Antispasmodics joined to diaphoretics appear to be the only remedies useful against this disease. Narcotics have seemed only to aggravate the affection, but bleeding and purgatives have been employed with some advantage in the beginning of the disease, according to the circumstances and temperament of the patient."

Modern study of ergotism

The result of the modern study of outbreaks of ergotism, including the minute record of individual cases, shows that there is no hard and fast line between the gangrenous and the convulsive forms; that the French epidemics, although, on the whole, marked by the phenomena of gangrene, have not been wanting in functional nervous symptoms, and that the German or northern outbreaks have often been of a mixed type.

Ergotism not yet extinct

Ergotism has by no means ceased in Europe. It is, however, now almost confined to the Russian Empire, in many parts of which it seems to be endemic. From 1785 to 1786, Kieff was ravaged by an epidemic, and between that period and 1838 there were eight distinct outbreaks of the disease in Russia. The year 1845 was very fertile in ergotism, and in 1881 there was a severe outbreak in Ekaterinoslav. In 1883 there was a further outbreak in Tomsk, in which thirty-six out of three hundred patients died, and as recently as 1888 there were many cases of the gangrenous type in the Government of Poltava, in which many of the sufferers lost a foot or a hand. Ergotism has also been observed in Abyssinia.

The comparative disappearance of this terrible scourge may be attributed to scientific investigation, to improvement in the social conditions of the people, and to the cultivation of rye and other cereals on drier soil under more favourable climatic conditions.

Linnæus erroneously ascribes ergotism to the radish

Many were the conjectures which were made by the early observers as to the cause of ergotism. Linnæus erroneously alleged that the malady was due to the radish (*Raphanus*), and thus his authority led to the name *Raphania* being given to ergotism. It does not appear, however, that Linnæus had ever visited the ravaged

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districts, and it has since been shown that the *Raphanus* is never poisonous.

Modern investigations

Modern science has shown us that ergotism is due to one or more poisonous principles, which are elaborated by the fungus *Claviceps purpurea*, and that contributory causes are starvation, misery and ill-health. Epidemics thrive only under conditions which are favourable to the growth of this parasite; that is, after a damp season, and particularly when a hot and dry summer has followed a very rainy spring, especially when the grain has been grown in marshy districts, and in the shade.

It has been conjectured that the two varieties of ergotism, the gangrenous and the convulsant, are caused by the varying amount of the active constituents present in ergot, and that the variability and strength of the preparations of ergot are due to the fact of the inconstant nature of the active principles present in the crude drug.

THE THERAPEUTIC HISTORY OF ERGOT

It is very probable that the physiological effects of ergot on the uterus were known to the "wise women" who performed the functions of the midwife from a period of great antiquity, and a secret of such value (from more than one point of view) would no doubt be most jealously guarded, and be handed down only by word of mouth.

Knowledge of its therapeutic properties in early times

It has been stated that its use was known to the "wise women" of the Highlands of Scotland at a very early period. They usually ordered it to be swallowed whole, in its natural state, giving from five to nine grains for a dose, but laying special stress on the point that the dose must first always be in odd numbers.

The earliest known allusion to the action of ergot on the uterus was made by Lonicer, in 1582, and again by Camerarius, in 1688, who records that women in certain parts of Germany were in the habit of employing spurred grain to accelerate parturition. Ray, in 1693, also refers to ergot as being considered an excellent remedy for "*Lochiorum fluxus*." No further reference seems to have been made to its medicinal properties until the year 1747, when Rathlauw, a Dutch surgeon, is believed to have used it in midwifery cases. That he undoubtedly used some medicinal agent of great obstetric value is evidenced by his own report of his methods: "I avail myself of a medicament," he states, "the second dose of which has never failed, in my experience, to excite true pains, or to change false ones to true, so that the efforts of the mother acting better on the child, the mouth of the womb dilates more. On different occasions, when only good pains were lacking, I have conducted to a happy end, by this means and without the help of any instrument, some most difficult labours."

Earliest known allusion to uterine action

Rathlauw used a drug supposed to have been ergot

Levret and others conclude that the drug so successfully used by Rathlauw was ergot of rye, and the former severely censures him for having kept secret the particulars of a method of treatment so useful to humanity.

About 1747, Salerne experimented with ergot on pigs, ducks and fowls, and, finding that they died of gangrene, he corroborated the statement of a previous observer, that fresh ergot was most virulent, and that after some months it gradually lost its poisonous properties.

Salerne's experiments

From that period there is no further mention of it being so used, until Parmentier, who had been investigating the subject, in an interesting letter in the *Observations sur la Physique*, gives the following account of its employment.

Parmentier on ergot in 1774

Letter from M. Parmentier, Apothecaire Major de l'Hôtel Royal des Invalides, to the Abbé Rosier, 1774:—

"In the number of letters, Sir, that I have had the honour of receiving on the subject of ergot, I have found nothing contrary to the opinion of M. Model on the origin and effects of this peculiar excrescence of rye. I am even bold enough to assert that they all confirm, as do my own experiences, that the accusations made on this subject have absolutely no foundation. However, as it is only after a long train of evidence that the opinion of the celebrated chemist of St. Petersburg will triumph, I think that I ought in the meantime to communicate to you certain observations, the singularity of which have appeared to me to be worthy of the attention of doctors and physicians. Here is what Madame Dupille,—whose chief occupation seems to be the alleviation of suffering,—here is, I say, what she had the goodness to write to me concerning ergot:—

'I read, Sir, in the last *Mercure*, of June, 1774, an extract from your works with respect to ergoted rye. A few years ago I heard mentioned the danger of this grain, and the terrible diseases it was said to have caused in Alsace, if I remember rightly, or in the neighbourhood. This information surprised me greatly, for from childhood I had known that it possessed a certain property from which I had never seen ill effects, nor had my mother, who had it taken to women who were in labour. I do not know from whom she learned this recipe. She had no other knowledge of medicine (nor have I) than the desire to help the needy. This is how she used to administer it, and how I myself have administered it on several occasions to various women, among others to the wife of the farmer of Bertichere, near Chaumont-Vexin, where I stay sometimes; she found that it did her much good.

'I pound this grain, which is commonly called *faux seigle*, to as fine a powder as possible. I then take a thimbleful of it, and make the patient swallow it in a spoonful of water or wine or broth, whichever is nearest to hand.

'The woman who has swallowed it ought to be delivered in a quarter of an hour. I only administer it, according to my mother's directions, when labour is too slow. The women who have taken it have never been ill afterwards.

'This, Sir, is all that I know, from my own experience and my mother's, about ergoted rye. If it can be of any use to you in your work I shall be delighted. Your essay has greatly reassured me with regard to the effects of this grain, which I feared to administer after all I had heard, and gives me the satisfaction of being able in a quarter of an hour to relieve from her pain a woman who is worn out by long and difficult labour: for my mother has assured me, and I myself have seen them delivered in a quarter of an hour.'

"I think I ought to add, Sir, that in several herborising expeditions which I have made to the outskirts of Paris, I have had occasion to remark this year that the ergot was much more common in the pieces of rye; that these were richer, and the ears not so full; that it is always on the edges of the pieces that it is found most abundantly; and that, finally, even before the complete maturing of the rye, this ergot at harvest time is so loose in the husk that the slightest movement of the sickle is sufficient to detach it, so that it is rarely that even a few grains of it reach the barn."

Desgranges strongly advocates the use of ergot

In 1777, Desgranges, a surgeon of Lyons, having met with several midwives at that period, both in Lyons and the surrounding district, who, from a traditionary knowledge were accustomed to employ, with no little mystery, the spurred rye in cases of lingering labour, at length made a great many trials of it, which for the most part were successful. He published several accounts of his observations and results in various journals, in which he specified, with great care, the peculiar circumstances in which ergot might be employed, and those cases also where it was contra-indicated. In spite of prejudices and opposition, he continued strongly to advocate its use, and to his perseverance we no doubt owe, to a very large extent, the use of ergot as a medicinal agent to-day.

When first announced in France, the use of spurred rye was known only in the department of the Rhone and some other departments on the frontier. But soon after the publication of its properties by Desgranges, it came to be used throughout the country.

The use of ergot spreads over Europe

Dittmer states that ergot was employed in different parts of Germany, and particularly in the environments of Ludwigsburg, in Würthemberg, where it was known and used by the midwives. It was soon tried in Italy by Bigeschi, of Florence, and Pistre, of Ferrara, who published directions to midwives for using it, and in France was advocated by Bourdot and Goupil of Paris, also Chevreuil of Angers. In Germany, its use was supported by Orjollet and Huchede, and in England, by Clarke, Davies and Merriman.

The use of ergot in America

In America, it appears somewhat doubtful whether its first introduction was due to Hosack or to Stearns. There is reliable evidence that Hosack was the first physician in America to employ ergot to arrest uterine hæmorrhage. On the other hand, it appears that Stearns was the first to use it in that country for accelerating delayed parturition. His suggestion is embodied in the following letter to a Mr. S. Akerly, written by Stearns from Saratoga County, on January 25, 1807:—

Letter written by Stearns

" In compliance with your request, I herewith transmit you a sample of the *Pulvis parturiens* which I have been in the habit of using for several years with the most complete success. It expedites lingering parturition and saves to the accoucheur a considerable portion of time without producing any bad effects on the patient. The cases in which I have generally found this powder useful are when the pains are lingering and have wholly subsided, or in any way incompetent to exclude the fœtus. Previous to its exhibition it is of the utmost importance to ascertain the presentation, and whether any preternatural obstruction prevents the delivery, as the violent and almost incessant action which it induces in the uterus precludes a possibility of turning. The pains induced by it are peculiarly forcing, though not accompanied by that distress and agony of which the patients frequently complain when the action is much less.

"My method of administering it is either in decoction or powder. Boil half a drachm of the powder in half a pint of water and give one-third every twenty minutes till the pain has commenced. In powder I give from five to ten grains. Some patients require larger doses, though I have generally found these sufficient; if the dose is large it produces nausea and vomiting.

"In most cases you will be surprised with the suddenness of its operation; it is, therefore, necessary to be completely ready before you give the medicine, as the urgency of the pains will allow you but a short time afterwards. Since I have adopted the use of this powder, I have seldom found a case to detain me more than three hours. Other physicians who have administered it concur with me in the success of the operation.

"The *modus operandi* I feel incompetent to explain. At the same time that it augments the action of the uterus it appears to relax the rigidity of the contracted muscular fibres. May it not produce the beneficial effects of bleeding without inducing that extreme debility which is always consequent upon copious depletion. This appears to be corroborated by its nauseating effects upon the stomach, and the known sympathy between the viscus and the uterus.

"It is a vegetable, and appears to be a spurious growth of rye. On examining a granary where rye is stored you will be able to procure a sufficient quantity from among that grain. Rye which grows in low wet ground yields in greatest abundance."

It is said that Stearns' attention was first called to ergot by observing its effects on some cattle that had eaten portions of the infected grain.

Stearns claims to be the discoverer of its properties

It is claimed that when he first used ergot he did not know of its previous employment for the same purpose in Europe, and Bigelow states, in *The New England Journal of Medicine and Surgery*, that it is to the best of our knowledge exclusively an American practice. So it is evident that its use in Europe at the end of the eighteenth century had not at that time spread to America. It is worthy of remark that in Stearns' letter, which has been quoted here, he never mentions ergot by name, and it is therefore quite probable that he was in ignorance of it, and may have at first heard of its administration in childbirth from some midwife of the backwoods in the course of his practice.

Prescott's experience

In June, 1813, Prescott, of Massachusetts, who followed Stearns as a pioneer in the use of ergot in America, published a dissertation on "The natural history and medicinal effects of the *Secale cornutum* or ergot," in which he treats of its operation exclusively upon the uterus.

He states: "I cannot say with Stearns, 'I have never been disappointed in my expectations of its effect.'" He administered ergot in the form of a decoction composed of half a drachm to four ounces of water, of which one-third was given for a dose.

How a physician tested ergot

A somewhat amusing use of ergot, which was made by a medical practitioner, is recorded in a letter which appeared in the *Lancet* in 1829. It states that an old woman brought to the doctor a favourite Malay hen, which to her great grief had been ten days in laying an egg.

The practitioner thought here was a chance to try the effects of the new ecbolic, and immediately thrust 30 grains down the fowl's throat, after which, he states, "the hen quickly laid, but whether *post hoc* or *propter hoc* let others determine."

EARLY METHODS OF ADMINISTERING ERGOT

The earliest known method of administering ergot was in its natural state in the form of fine powder. In this manner it was given by Desgranges and Stearns, and was called by the latter *Pulvis parturiens*, and was also known as *Pulvis partum accelerans.* By Desgranges it was termed "poudre obstetrical," and by Bordot "poudre ocyotique." By some it was recommended to be given in "good generous wine"; by others "mixed with milk or cloves or with the distilled waters of nutmeg or mint." Balardini advises that it should be swallowed with white wine, while Bordot frequently prescribed it in combination with powdered nutmeg and sugar. The dose given varied according to the circumstances of the case, and the susceptibility of the patient. The maximum prescribed by Stearns was ten grains, but it was frequently given by other practitioners in 90-grain doses, in a wineglassful of barley water, cinnamon or orange water.

Goupil relied on the following formula:—

℞ Secalis Nigri Pulv.,	dr. i.
Syrupi Simplicis,	oz. ½.
Ol. Menthae Essent.,	gutt. iij.

Misce in mortario.

To be given in doses of a spoonful at intervals of ten minutes

Stearns and Gill suggested the admixture of opium with ergot in the proportion of one grain of the former to thirty of the latter.

Another early method of administration chiefly employed in America, was in the form of an infusion, commonly called "Tea of black rye." It was thus used largely by American midwives who prepared it by infusing one drachm of the powdered ergot in a wineglassful of boiling water and allowing it to stand until it became cold. The liquid was then strained and divided into two equal portions. The first was administered when necessary, and the second after the interval of one hour if required. This infusion was recommended by Chevreuil and Akerly, although Walter considered it too weak, and suggested using an infusion double that strength.

"Tea of black rye"

"Decoctum parturiens"

Another form of administering ergot was the decoction which was made of the same strength as the infusion, but was boiled for a quarter of an hour, and then allowed to cool. This was known as *Decoctum parturiens.*

Madame Lachapell gave ergot in the forms both of infusion and decoction, and administered the liquid, without straining, in doses of two drachms.

Foote's method was to boil up the entire grain and give the resulting decoction, in tablespoonful doses, at short intervals. Desgranges recommended roasting the powdered ergot gently before the fire, and also states that he gave the black external part only in doses of four to six grains, without any of the inner substance, and that these small doses proved equal in effect to one drachm of the entire grain. Villeneuve mentions that he found ergot useful as an enema, when it could not be borne by the stomach, and in this way it might be used in much larger quantities. He employed from two to three drachms of the powder, boiled in half a pint of water, and strained off for use. Should the first enema fail, the second or third might be given.

A formula much used in France, devised by Pierquin, was known as "ocytic potion." It was made as follows :—

℞ Spurred Rye,	1 drachm.
Simple Syrup,	3 ounces.
Tincture of Opium,	20 drops.
Essence of Bergamot,	*q.s.*

The hypodermic injection of extract of ergot was first employed for aneurisms by Professor Langenbeck, of Berlin, in 1869, but, owing to the irritation set up, this form of administration was not met with favour.

Ergot first used hypodermically

THE COLLECTION OF ERGOT

Ergot is chiefly exported from Russia, Austria, Germany and Spain.

Rye is practically the staple cereal of Russia, and from the annual crop, which is very large, a considerable amount of ergot is collected. The sowing time is during July and August, and the grain is harvested in June and July. During threshing time the ergot is separated out and collected, then simply dried in the air. After drying it, the peasant collectors pack the ergot in small parcels which they dispose of to the dealers, by whom it is carried to the towns and resold to the exporters and druggists. Tomsk, Omsk, Samara, Viatka, Siberia and Bessarabia are the principal Russian trading centres for the drug.

The increase in the quantity of ergot exported from Russia has been very great in recent years. In 1900, 45·04 tons of the value of 19,650 roubles were exported from the country, while in 1906, 215·30 tons of the value of 162,233 roubles was the total amount.

All investigators agree that the great value of ergot depends on the freshness of the drug, and that if the fungus is collected two or three weeks before the rye is fully ripe its action is much greater.

Keller gives the following statement of the alkaloidal value of ergot grown in different countries of Europe:—

Russian contains 0·245 per cent. alkaloid; Austrian, 0·225 per cent.; Spanish, 0·205 per cent.; German, 0·13 to 0·157 per cent.; Swiss, 0·095 per cent.

After examination by Keller's process, Dohme gives the following percentages of cornutine in the samples taken by him: Spanish, 0·29; Russian, 0·18; German, 0·15.

CHEMICAL HISTORY

The somewhat mysterious origin of ergot appears to have attracted many investigators, but, owing mainly to lack of knowledge at the period in which they worked, the earlier observers only succeeded in isolating some of its inert constituents. The physiologically active preparations they were able to obtain were simply crude resinous mixtures, which their discoverers regarded as acids or alkaloids according to their methods of preparation.

Pettenkofer, when examining ergot in 1814, obtained some crystals which he thought resembled those of morphine. Vanquelin next made a chemical examination in 1816, and he was followed by Combes, who, in 1826, asserts that he found starch, but could not separate any active principle; and down to about 1830 nothing was known of its chemical composition.

Wiggers' investigations

The first reliable investigation of ergot was made in 1831, by Wiggers, who found it contained 35 per cent. of oil and a crystalline wax-like substance, which he termed cerin; he also proved that starch and hydrocyanic acid were absent, and described a resin, soluble in alcohol but insoluble in ether and water, which he termed ergotin. From feeding experiments on cocks he concluded that the toxic properties of ergot were wholly due to the resin.

Bonjean's researches

In 1840, the Pharmaceutical Society of Paris offered a prize for the best essay on ergot of rye, and a research was made by Bonjean, who stated that he found that ergot owed its activity to two principles, one of which he contended was a powerful poison and the other a "salutary medicine." The former he called "Oil of Ergot" and the latter

"Ergotin," and for his research he was awarded a gold medal. Ergotin soon came into general use as a remedial agent in various diseases, such as hæmoptysis, dysentery, hæmorrhoids, etc., and in 1855 was largely employed during the Crimean War with apparent success in chronic diarrhœa following cholera.

In France ergotin became the fashion, and appears to have been regarded about that time as a panacea for the majority of ills. It was exhibited in the form of ergotin dragees, ergotin injections, ergotin lemonade, which was recommended for scurvy, and in many other forms.

Tanret isolates ergotinine

The first approach toward the isolation of a pure active principle from ergot was made by Tanret, who in 1875 described the crystalline alkaloid "ergotinine," and an amorphous alkaloid which he regarded as a mere physical modification of the crystalline. Independently and almost simultaneously, Kraft also isolated the amorphous alkaloid, and by naming it hydro-ergotinine, suggested its relation to the crystalline ergotinine.

Kobert's cornutine

According to Kobert's investigations, in 1890, the most active constituent of ergot is cornutine, which, together with sphacelinic acid, is contained in an alkaloid extract after the removal of oil by ether. He also stated that no aqueous extract of ergot is of any therapeutic value after being made nine months, but Kobert's observations were not only questioned, but totally contradicted by Tanret.

Keller's observations

According to Keller's investigation, in 1896, ergot contained but one base, and Kobert's cornutine, Tanret's ergotinine, and Dragendorff and Podwyssotski's picrosclerotine were simply different forms of the same body.

In 1897, Jacobj gave the name of sphacelotoxin to a substance of a resinous nature which he obtained from ergot, and which he regarded as a specifically active constituent of the drug.

Although a good deal of clinical evidence was adduced to support Tanret's view that in ergotinine he had isolated the active therapeutic principle of ergot, the experiments conducted by Kobert and others showed the pure crystalline alkaloid to be inert. Recently this apparent discrepancy has been explained by the isolation by Barger and Carr, in the Wellcome Physiological Research Laboratory, of the highly active alkaloid, ergotoxine, which, although itself amorphous, can, in the form of its crystalline salts, be prepared in a state of chemical purity. It has since been shown that ergotoxine is the hydrate of Tanret's crystalline ergotinine, and that either can easily be converted into the other, and also that the active principles prepared both by Kobert and Jacobj, owe their activity to the presence in them of ergotoxine.

Ergotoxine discovered in the Wellcome Physiological Research Laboratory

Both laboratory experiment and the results of clinical trial have already made it evident that ergotoxine in suitable doses produces the effects for which ergot is prescribed.

The great value, however, of this principle as a medicinal agent is due to the fact that the dose can be regulated with a degree of accuracy which has been impossible in the past when only extracts and similar preparations of the crude drug were available.

Its great value as a medicinal agent

The results obtained with the official liquid extract, and with other preparations of ergot hitherto in use, have been variable and uncertain. This has been due to ignorance of the properties and active constituents of the drug, which has of necessity prevented the elaboration of correct pharmaceutical methods.

Unreliability of former crude preparations

The isolation of the active alkaloid ergotoxine now renders possible, for the first time, the production of an ergot preparation of definite strength. A chemical method of standardising such a product has not yet been devised, but the activity, as represented by the ergotoxine content, can be gauged with extreme accuracy by physiological tests.

Accurate standardisation impossible by old methods

Various methods of physiologically standardising ergot have been suggested. The production of gangrene in the cock's comb, described by various observers since the seventeenth century, has been used as a test of activity. This test tells little more than that a certain specimen of ergot is or is not active. No accurate standardisation of pharmacological or therapeutic value is possible by means of this test.

The rise of blood-pressure following the intravenous injection of a standard dose of ergot is also suggested as an indication of activity. Such a method alone is neither accurate nor complete. It furnishes at most a rough test of the activity of such a preparation as the official liquid extract.

Preparations containing ergotoxine can, however, be accurately assayed, by physiological means, for their ergotoxine content. This is rendered possible by observation of the characteristic action of the alkaloid on the terminal motor elements of the sympathetic nervous system.

Importance of ergotoxine to the physician

The importance of this is evident. The activity of ordinary preparations cannot be gauged. Different specimens have been shown to vary from inertness to an activity which is believed to be the cause of the sporadic cases of ergot-gangrene which have been reported as following medicinal doses.

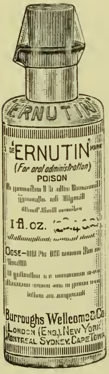
With the discovery of ergotoxine, and the consequent improvement in preparations, the confidence of the practitioner in ergot is restored. He is now able to prescribe a standardised product of exact strength, in accurate doses, and obtain definite results.

A Chronological Table of the Chief Events in the History of Ergot

B.C.	
2500	Probable allusion to ergot on Babylonian tablet.
660	Probable allusion to ergot on Assyrian tablet.
300 ca.	Probable allusion to ergot in the Hindu Yasna.
A.D.	
857 ca.	First recorded epidemic of ergotism.
944	Epidemic of ergotism in Aquitaine, Limousin, Angoumois and Perigord.
950	Allusion to the poisonous properties of ergot made by Abu Mausur Muwaffak.
957	Epidemic of ergotism in Paris.
1039	Epidemic of ergotism in Metz.
1089	Epidemic of ergotism in Lorraine.
1096	Sigebert records an epidemic following the consumption of damaged crops.
1129	Epidemic of ergotism in Paris.
1582	Lonicer alludes to ergot, describes its appearance in the ears of rye, and first notes its uterine properties.
1588	Thallius describes ergot and mentions its hæmostatic properties.
1596	First suggestion that ergot was probably the cause of the epidemics of *ignis sacer*.
1630	Thuillier calls attention to the fact that ergot was the cause of the epidemics.
1648–75	Ergotism prevalent in Voigtland.
1660–74	Ergotism prevalent in Aquitaine, Gattinais and the Sologne.
1682	Bernier notes the fact that ergot was the cause of dangerous diseases in the Sologne.
1688	Camerarius records the medicinal use of ergot by women.
1693	Ray describes the growth of ergot and alludes to its medicinal effects.
1702	Epidemic of ergotism in Freiburg.
1709	Epidemic of ergotism in Berne, Lucerne and Zurich.
1710	Epidemic of ergotism in Russia.
1716	Ergotism prevalent in Saxony and Lusatia.
1717	Epidemic of ergotism in Germany and Silesia.
1746–7	Severe outbreaks of ergotism in Sweden, Russia, Sologne, Les Landes, Artois and Flanders.
1747	Rathlauw stated to have used ergot in midwifery practice.
1762	A case of ergotism in England.
1771	The identity of *ignis sacer* with gangrenous ergotism established.
1774	Parmentier investigates ergot.
1785	Epidemic of ergotism in Kief.
1807	Stearns publishes his experience of the use of ergot in America.
1814	Pettenkofer makes a chemical examination of ergot.
1816	Vanguelin makes a chemical examination of ergot.
1831	Wiggers describes a resin which he terms "ergotin."
1840	Bonjean investigates ergot and extracts oil of ergot and ergotin.
1845	Outbreak of ergotism in Russia.
1875	Tanret describes ergotinine, and Kraft isolates hydro-ergotinine.
1890	Kobert investigates ergot and isolates cornutine and sphacelinic acid.
1896	Keller investigates ergot.
1897	Jacobj isolates sphacelotoxin.
1907	Barger and Carr discover ergotoxine.

TRADE MARK 'ERNUTIN' BRAND PRODUCTS

Present the active therapeutic principles of Ergot



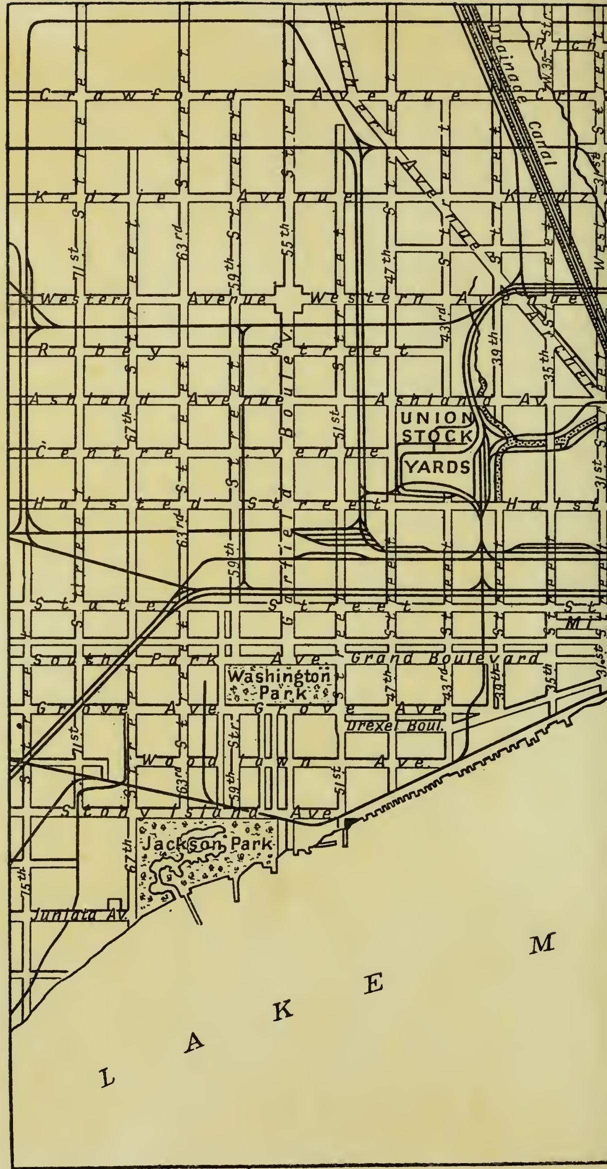
'Ernutin' for oral use

THE various extracts and preparations of ergot in ordinary use consist almost entirely of inert or harmful matters having little or none of the therapeutic action desired. Those preparations which exhibit the characteristic effects of ergot on the blood-pressure and the uterus, in laboratory experiment or clinical use, owe their activity to certain specific active principles, the effect of which is in such preparations obscured and complicated by the depressor constituents.

'ERNUTIN' products present the active therapeutic principles of ergot, chief of which is the alkaloid ergotoxine, in a state of purity which hitherto has never been approached. The action of ergotoxine on the sympathetic nervous system, as indicated by H. H. Dale in his papers on this subject (*Journal of Physiology*, vol. xxxii. p. 58 [*Proc. Phys. Soc.*, 1905]; vol. xxxiv. p. 163, 1906), affords a standard for the measurement of activity. 'Ernutin' products are physiologically standardised by observation of the effects on the vasomotor functions of the sympathetic nervous system.

Method of standardisation

'Ernutin' (Oral) is issued in 1 oz. and 30 c.c. bottles



Crawford Avenue
Kedzie Avenue
Western Avenue
Robey Street
Ashland Avenue
Centre Avenue
Halsted Street
State Street
South Park Ave. Grand Boulevard
Grove Ave.
Drexel Boul.
Woodlawn Ave.
Stony Island Ave.
Juniata Av.
Washington Park
Jackson Park
UNION STOCK YARDS
Garfield Boulev.
Archer Ave
Drainage Canal
W.35
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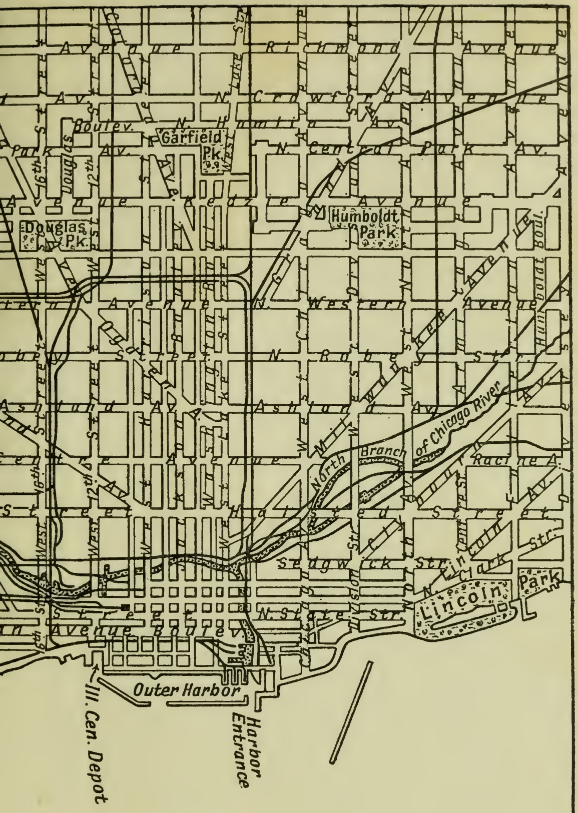

CHICAGO, IN 1908.